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PATHOLOGIC CHANGES OF SENILE TYPE IN CHARCOT'S DISEASE *

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As the histopathology of nervous affections becomes more precise, it becomes apparent that most processes of disintegration in the nervous system have no specific significance either as a whole or as to the cytologic elements which they include. It seems that, in the absence of a definite etiologic agent, the anatomic characteristics of a syndrome are brought about by the topography and evolutionary sequence of the lesions rather than by their histopathologic pictures.

We discussed this recently [1] in relation to the perivascular formulas occurring in the course of various phenomena of nervous system disintegration. Whatever is the origin of nerve destruction, whatever the cause—trophic, circulatory or infectious—the interstitial tissue of the nervous system reacts in an identical manner; the histopathologic picture thus produced is not pathognomonic of a given disease. In a work on disintegration of the nervous system,[2] one of us has pointed out the great complexity of this problem.

A study of the cerebral histopathologic changes in Charcot's disease furnishes the opportunity to return to this question of histobiology apropos of the presence in the cortex of degenerative, cellular or vascular lesions which have hitherto been accepted as specific for the brains of normal or pathologic senility. The following two cases of amyotrophic lateral sclerosis showed characteristic senile formations in the cortex.

REPORT OF CASES

CASE 1.—Mme. H. Marie, aged 46, a housewife, who at the age of 9 had had a serious infectious illness (typhoid or scarlet fever), was the mother of six

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1. Bertrand, Ivan, and Van Bogaert, Ludo: Les périvascularites en histopathologie nerveuse, Folia neuropath. eston. **3-4**:102, 1925.

2. Bertrand, Ivan: Les processus de désintégration nerveuse, Paris, Masson et Cie, 1924.

children, two of whom died young. Her present illness began at the age of 43 with paretic phenomena in both legs and stiffness in the left leg. A month later, the same heaviness and stiffness appeared in the left arm; the patient became awkward in the use of her hands but could still attend to her housework. A year and a half later, the right leg became affected, walking became difficult, and the patient felt a certain fatigue in the back, the lumbar muscles being tender to pressure and walking painful. The weakness became aggravated and the left arm began to atrophy. Soon after, the right arm became affected; two and a half years after the onset of the illness there appeared severe muscular twitching in the arms and legs, and a feeling of swelling in the back of the throat. In ten days a characteristic bulbar syndrome appeared with disturbances in phonation and deglutition.

Examination.—Motility was retained for some movements of the upper limbs: flexion of the wrist and fingers, supination of the forearm, and elevation of the shoulder on the right; on the left almost complete paralysis was present, except for the delicate movements of the fingers. Slight muscular power was preserved in the flexor muscles of the lower limbs; power was much diminished in the extensor group, the two sides being equally affected. Considerable paresis was noted in the back movements; flexion was greatly diminished, and resistance to extension was almost nil. The lower abdominal reflexes were weak, the middle and upper ones intact.

There was complete atrophy of the muscles of both hands, of the supinator muscles of the arms, and of the deltoid and scapular muscles on the left. The bicipital reflex was normal on the right, very active on the left side. The radial periosteal reflexes were very active on both sides; the abduction-in-supination reflex was present in the left limb.

There was slight atrophy in the lower limbs. The knee reflexes were very active with patellar clonus, but there was no ankle clonus. The plantar reflex was of extensor type on both sides.

Numerous fibrillations were observed in the tongue, with paresis of protrusion and lateral movement. Power was diminished in the muscles of mastication and of the peribuccal, pterygoid and orbicularis palpebrarum muscles, with much fibrillary twitching in the small muscles of the chin and in the platysma.

Difficulty was experienced in swallowing and speaking, but the laryngeal, velopalatine and pharyngeal muscles were intact.

The Wassermann reaction with the blood was negative.

Course.—Little increase occurred in the atrophy of the limb muscles, but stiffness increased and prevented all movements. The right leg went into a position of hyperextension, the foot into equinovarus. The voice became more feeble and nasal.

After a period of thirteen and a half months, during which the neurologic situation remained unchanged despite the fact that the patient grew very thin, the disease resumed a rapid course and almost total atrophy appeared; tube feeding became necessary; attacks of dyspnea occurred, and death followed.

The duration of the disease was forty-nine months.

Necropsy After Formaldehyde Fixation in Situ.—No macroscopic changes were found in the meninges or vessels. After the pia was removed a discrete atrophy of the paracentral lobule, the precentral and second frontal convolutions and a segment of the first frontal gyrus was found. Atrophy was present in the cervical region of the spinal cord.

Anatomic Study.—Spinal Cord. Very few cell lesions were present in the dorsal region. Marked lesions existed of the anterior radicular groups of cells at

the level of the cervical enlargement; all the cells had disappeared except those of the sympathetic group in the lateral horn. In the lumbosacral region a few radicular cells remained.

A moderate degree of gliosis was present around the emergence of the posterior roots.

With Weigert-Pal staining, degeneration of the crossed pyramidal tract could be followed in the dorsal and lumbosacral regions to the second sacral level; in the lower cervical cord, degeneration was found in the crossed pyramidal tract, the adjacent fundamental tract and the posterior third of the direct cerebellar tract; there was slight pallor of the direct pyramidal tract in the upper cervical cord; the lesions were limited to the lateral column, the anterior one being intact.

Numerous granular bodies and Marchi bodies were found in both lateral columns, but principally in the right.

The vascular lesions differed in the white and gray substances. In the gray matter there were recent lesions, with lymphoid reactions, in the center of the anterior horn and in the substantia gelatinosa of Rolando. In the white matter perivascular disintegration with light halos of tissue rarefaction was observed. In the posterior columns there were fibrosis and hyaline degeneration of the vessels with numerous juxtavascular amyloid bodies.

Medulla. Lesions of recent type were found in the retropyramidal nucleus, the substantia reticulata, the nuclei of the vagus, the posterior columns and the region of the restiform bodies. Cellular rarefaction had occurred in the nuclei of the hypoglossus and there were old cell lesions in the arciform nuclei, marked degeneration of the pyramids, pallor of the external interolivary fibers and absence of the fibers from the hypoglossal nuclei. In the pyramids, Marchi specimens showed great abundance of granular bodies, particularly on the right.

Pons. Degeneration of the pyramidal tract could be followed in Weigert and Marchi preparations. Acute cell lesions were present in the motor nuclei of the trigeminus and in the substantia reticulata.

Peduncles. These were degenerated in the middle quarter with involvement of certain cellular elements of the third nerves.

Internal Capsules. In Marchi preparations, granular bodies were observed in the whole lenticulo-optic segment; a few were present in the retrolenticular segment and in the knee. A few frontothalamic fibers in the anterior limb showed fine products of distintegration. In Weigert-Pal specimens there was pallor of the posterior third of the lenticulo-optic segment.

Corpus Callosum. Numerous granular bodies were present in the knee and body.

Cortex and Centrum Ovale. These were subjected to detailed study,[3] the results of which may be summarized as follows:[4]

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3. Van Bogaert, Ludo: Les lésions cérébrales dans la sclérose latérale amyotrophique, Arch. internat. d. méd. expér. **1**:341, 1925.

4. For the sake of uniformity we have adopted the terminology of C. and O. Vogt (Allgemeine Ergebnisse über Hirnforschung, J. f. Psychol., 1919). These authors employ, to designate the cortical layers, the figures established by Brodmann, using Roman figures to indicate the cell layers and Arabic figures for the corresponding fiber layers. C. and O. Vogt have shown further that the layers act toward pathogenic agents as "topistic" units of exquisite sensitivity, and may be affected by them either singly or in combination. When the noxious agent attacks only one layer the lesion will be described as "monotopic;" when it attacks several layers it will be called "polytopic." In the latter case some layers may be more

1. Cytoarchitectonic lesions: in the frontal region—polytopic lesions of type II-V with hypergliosis in (II)-III-IV-V. These changes predominated in the lower prefrontal fields.

In the precentral region—monotopic lesions in III, hypergliosis in II-III-IV-V-VI. They were more pronounced on the left; on the right they did not affect field 4.

In the postcentral and temporal regions of both sides—hypergliosis of varying types and severity. In the parietal region of both sides—polytopic lesions of type III-V-VI.

In the occipital region—monotopic and heterotopic with gliosis of II *inf.*—III-V in one hemisphere.

In the hippocampus of both sides—rarefaction of the pyramidal cells of the fascia dentata of the alveus, neuronophagia with diffuse reaction of satellite cells in VI, and in the hippocampal cortex polytopic lesions of type II-III-V-VI with analogous hypergliosis.

The architectonic lesions predominated in the anterior parts of the brain and overflowed into the parietal areas. The hypergliosis extended throughout the cortex. The lesions were more severe in the left hemicortex.

2. Myelotectonic lesions: The lesions were localized in front of the rolandic fissure. In the whole prefrontal tract (except Brodmann's area 9 on the left) the horizontal fibers alone were rarefied, especially those of 1*a*, 3*a* and 4 layers and the deep fibers.

The lesions of the precentral convolution were severe and extensive; those of the postcentral convolution were discrete and limited to the anterior half of the gyrus in the radial fibers.

3. Recent degenerative lesions: No granular bodies were found in the cortex nor the centrum ovale.

The most remarkable feature, outside of a rather diffuse cerebral disintegration, was the presence in the first frontal gyrus and in Ammon's horn on both sides of senile plaques, with various forms of cell degeneration of senile type and atrophy of the cortex. We shall describe these more fully later.

Case 2.—B., a man, aged 59, a packer, whose family and past histories were unimportant, noticed tiredness in walking or climbing stairs. At the end of four months there was a paraparesis of the lower limbs with a steppage gait. A little later, pain was experienced in the right hand and forearm, and progressive atrophy of the arm and forearm muscles, and later of the shoulder muscles, developed. On the left side pain and paresthesia with wasting developed progressively.

Neurologic Examination.—Amyotrophy was marked on the right side with a typical Aran-Duchenne hand; it was beginning in the left thenar and hypothenar eminences, the inteossei and the biceps muscle. The right sternocleidomastoid muscle was thinner than the left. Occasional fibrillary twitching was observed in the trapezius and deltoid muscles of both sides.

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slightly damaged, and these will be indicated by placing the figures in parentheses. This method avoids tiresome repetitions; the different cytoarchitectonic findings in each convolution are condensed into a schematic formula. Suppose, for example, that study of a level in the first frontal convolution reveals rarefaction of the large pyramidal cell layer (III*b*) and of the ganglionic layer (V), with, in addition, a discrete lesion of the medium and small pyramidal cell layer (III*a*); we shall identify this pathologic complex by the formula: polytopic lesion of type III*b*-V-(III*a*).

In the lower limbs, rather marked amyotrophy was present in the peroneal and tibial muscles of both sides and in the right quadriceps. Motor power was retained in the extensor muscles. Flexion of the foot was badly maintained against resistance on both sides. The reflex of the hip on the pelvis was greater on the right than the left where it, nevertheless, was deficient.

In the right arm, motor power was much involved, except for flexion of the first and second phalanges; power was preserved in the adductors of the wrist and the elevators of the shoulder. In the left arm power was preserved for all movements.

Very active reflexes were present in both upper limbs with polykinetic responses of the wrists on both sides. The knee reflexes were marked; Achilles reflexes were brisk; clonus was obtained at the ankle and knee on both sides. The plantar reflexes were of flexor type; the abdominal and cremasteric reflexes were present.

No sensory or cerebral disturbance was found.

Course.—Forty months after the onset there appeared slight paretic disorder of the facial and hypoglossal nerves with occasional fibrillary twitching, trismus and jaw clonus.

Death occurred at the end of fifty-three months as a result of aspiration bronchopneumonia.

Necropsy.—No macroscopic changes were observed in the brain.

Anatomic Examination.—Spinal Cord. Lesions of the Nissl bodies predominated in the more posterior groups of the external mass of cells, except in the lumbosacral enlargement where the central and antero-external groups were equally affected. The cells of the dorsal segments were but slightly affected. The fibers of the horns were few and slender.

In the dorsolumbar and lower cord, the direct pyramidal tract and the parts adjacent in the fundamental tract were degenerated. In the middle and upper cervical levels, the direct cerebellar tract was affected on both sides, the direct pyramidal and the fundamental tract of the anterior column were also affected by degeneration to such a degree that the pale zone reached anteriorly to the periphery of the cord.

In Marchi preparations many granular bodies were present in the crossed pyramidal tract, and also in the cerebellar and Gowers' tracts. Degeneration of the external bundle and abundant osmophilic products were present in the posterior column and Burdach's column as far down as the fifth lumbar segment. The vessels showed considerable enlargement of adventitial spaces with a few rare lymphocytes, new formation of capillaries with secondary fibrosis in the posterior columns, especially in Burdach's column, and numerous perivascular amyloid bodies.

Medulla. Here there were lesions of cell sclerosis with vacuolar and lipoid degeneration in the restiform bodies, the external olivary nucleus and the lateral nucleus of the medulla; recent chromatolysis was present in the nucleus of Goll; cell alteration and diminished number of cells were present in the twelfth nucleus, and to a less extent in the seventh nucleus.

Long standing degeneration was present in the pyramidal tracts and the arciform fibers, and there was pallor of the external and internal systems of the olive, of the nucleus and root of the hypoglossus, of the tract of Goll, and of the descending fibers of the ninth nerve; granular bodes were present in the area of the pyramids, the fundamental tract of the medulla between the substantia gelatinosa of Rolando and the substantia reticulata grisea anteriorly, and in the left arciform nucleus.

The interolivary white matter, the internal and external olivary systems as well as the root of the twelfth nerve and the restiform bodies showed a few osmophilic products.

Pons. The pyramidal degeneration was seen in Weigert and Marchi preparations. There were no nuclear lesions.

Peduncles. Very few lesions were observed in Marchi or Weigert preparations.

Internal Capsules. Pallor of fibers was found in the whole of the lenticulo-optic segments and in the fiber system of Forel-Omifrovicz. Granular bodies were present in the posterior third of the lenticulo-optic segment, and products of disintegration in Marchi preparations in the fibers which leave the pyramidal tract to penetrate the caudate nucleus and lenticular nucleus.

Cortex and Centrum Ovale. These were studied elsewhere; following is a summary of the findings:

Cytoarchitectonic Findings: in the frontal and agranular precentral region—polytopic lesions of type II-III-(IV-VI) with diffuse hypergliosis in III-VI.

In the gigantopyramidal precentral region there were few cell lesions, but hypergliosis was present in II-VI. In the postcentral region, and in the third temporal and postcentral gyri there were polytopic lesions of type II-III, with hypergliosis somewhat disseminated but marked in III-VI.

The architectonic lesions involve the whole cortex except the occipital and temporal regions. The gigantopyramidal areas were quasi-intact, the lesions slight. The superficial tangential fibers of 1-3 were diminished in the whole precentral area; otherwise there were no appreciable changes.

No granular bodies were found in the cortex or centrum ovale.

We wish to emphasize the disorder of structure in the left hippocampus: marked cell rarefaction, presence of senile plaques and cell lesions of senile type; and in the centrum ovale: vascular, état criblé and lacunar lesions. These will be discussed in detail later.

SENILE PLAQUES

The senile plaques, discovered by Blocq and Marinesco [5] and isolated by Redlich,[6] have been described in great detail by Fischer.[7] An excellent report on them is that of Ley [8] on the pathologic anatomy of senility published in 1922. Their significance has been much discussed. Alzheimer [9] described them in a group of senile dementias, a group to which Kraepelin [10] gave the name "Alzheimer's disease."

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5. Blocq and Marinesco: Sur les lésions et la pathogénie de l'epilepsie dite essentielle, Semaine méd., 1892, p. 445.

6. Redlich: Ueber miliäre Sklerose der Hirnrinde bei seniler Atrophie, Jahrb. f. Psychiat. u. Neurol., 1898; quoted by Léri.

7. Fischer: Miliäre Nekrosen mit drüsigen Wucherungen der Neurofibrillen, eine regelmässige Veränderung der Hirnrinde bei senile Demenz, Monatschr. f. Psychiat. u. Neurol. **22**:361, 1907.

8. Ley, R.: Étude anatomique de la sénilité, Livre jubilaire de la Société Belge de Neurologie et Psychiatrie, Imprim. méd. et scient., 1922, p. 32.

9. Alzheimer: Ueber eigenartige Krankheitsfälle des späteren Alters, Ztschr. u. histopath. Arb. ü. die Grosshirnrinde **4**:267, 1911.

10. Kraepelin, Emil: Einführung in die psychiatrischen Klinik, ed. 4, Vienna, Emil Deuticke, 1924.

Fischer [11] first considered them to be the anatomic substratum of Wernicke's presbyophrenia, and later of presbyophrenic dementia,[12] which he contrasts with simple senile dementia. Spielmeyer demonstrated them in the latter.[13] Haunted by an idea of the specificity of these formations, Sigg [14] and Schoenfeld [15] held them to be constant in agitated presbyophrenias.

Simchowicz [16] paid less attention to their presence than to their number, arrangement and topography. Fuller [17] believed them merely more frequent in senile dementia than in other diseases, and Huebner [18] finally put forth the idea that their presence is in no way specific. It is to this idea that many present investigators are rallying and we may quote Ley's [19] conclusion: "The senile plaques may be found in considerable numbers in normal subjects, they are neither distinguishable by number, aspect, nor distribution from those described in senile dementias. Even very numerous plaques may not give appreciable symptoms during life; they are the expression of a general senile process."

The most recent work of Theofil Simchowicz,[20] to whom we owe excellent articles on senile plaques, ends with an analogous conclusion, with which we agree, at least in the second part: "from a clinical point of view, as from an anatomic point of view, senile dementia does not necessarily differ from normal old age and constitutes merely its highest degree." And further "the areas of miliary sclerosis are the only absolutely characteristic and typical lesions of the senile cortex; they become more numerous as other senile lesions become more pronounced."

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11. Fischer: Histopathologie der Presbyophrenie, Monatschr. f. Psychiat. u. Neurol. **22**:361, 1907.

12. Fischer: Die presbyophrenie Demenz, dessen anatomische Grundlage und klinische Abgrenzung, Ztschr. f. d. ges. Neurol, u. Psychiat. **10**:371, 1910, and **12**:99, 1912.

13. Spielmeyer: Ueber die Alterserkrankungen des Zentralnervensystems, Deutsche med. Wchnschr. **31**, 1911.

14. Sigg: Versuch einer retrosp.; Diagnose der senilen Psychosen nach dem Drüsenbefund, Ztschr. f. d. ges. Neurol. u. Psychiat. **24**:453, 1914.

15. Schoenfeld: Vorkommen und Bedeutung der drüsigen Bildungen in der Hirnrinde, Monatschr. f. Psychiat. u. Neurol. **36**:342, 1914.

16. Simchowicz, T.: Histologische Studien ueber die senile Demenz, Histol. u. histopath. Arb. ü. die Grosshirnrinde **4**:267, 1911.

17. Fuller: A Study of Miliary Plaques Formed in the Brain of the Aged, Proc. Amer. Med.-Psychol. Assn. **18**:2, 1911.

18. Huebner: Zur Histopathologie der senilen Hirnrinde, Arch. f. Psychiat. **46**:596, 1909; Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte **80**:391, 1908; Arch. f. Psychiat. u. Neurol. **46**:28, 1910.

19. Ley (footnote 8, p. 34).

20. Simchowicz, T.: Sur la signification des plaques séniles et sur la formule sénile de l'écorce cérébrale, Rev. neurol. **31**:221 (Feb.) 1924.

The varied appearances of senile plaques have often been described; the accompanying figures show their diverse morphology better than a long explanation. In our preparations we were able to observe all transitions between the diffuse argentophile substance lying among fibrous neuroglia, plaques lying next to blood vessels in bands (fig. 1) and well formed oval (fig. 2) or polycylic plaques due to confluence (fig. 3). Young diffuse plaques without pseudonuclear masses are most frequently found.

Another type is an over impregnated network with dense meshes without inclusions. This network may become rarefied; vacuoles may

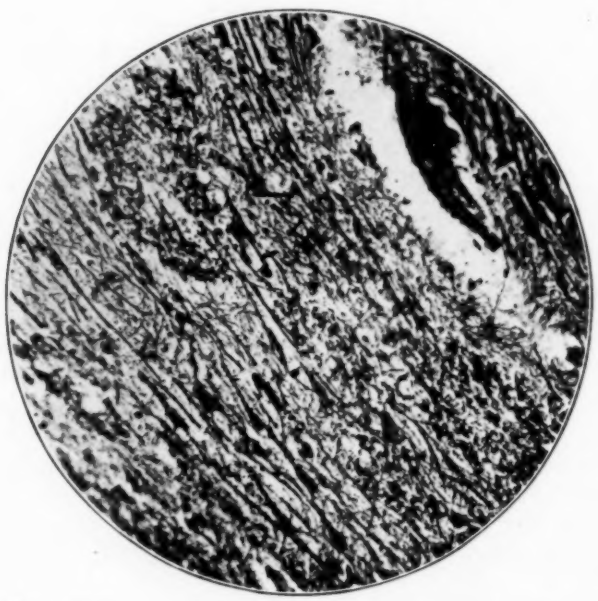

Fig. 1.—Diffuse paravascular bands of argentophil substance.

appear in it containing globular formations, or there may be axons showing button-like enlargements due to irritation (fig. 4). The nerve fibers near plaques may show phenomena of "neurocladisme." They may on account of their great number give to the plaque a more or less filamentous, ameboid appearance shown by Tinel.[21] These plaques should not be confused with the debris "en bouquet" of Alzheimer cells. All these appearances have already been described by Fischer [22] in a classification which is perhaps a little too forced. However, one

21. Tinel: Les processus anatomopathologiques de la démence sénile, Rev. neurol. **31**:26 (July) 1924.

22. Fischer (footnote 11, p. 365).

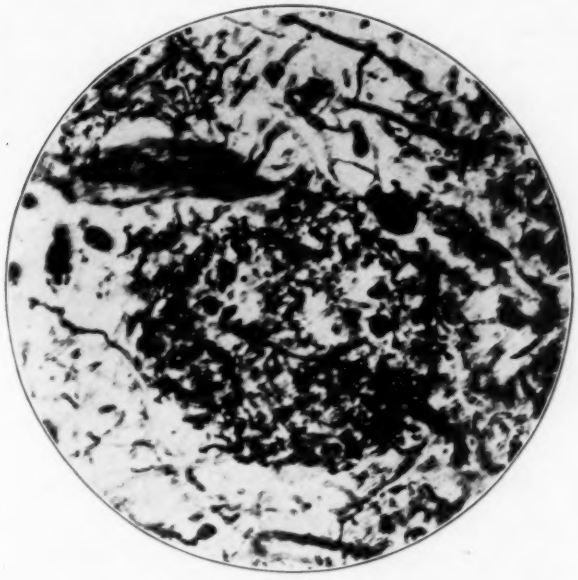

Fig. 2.—Round senile plaque.

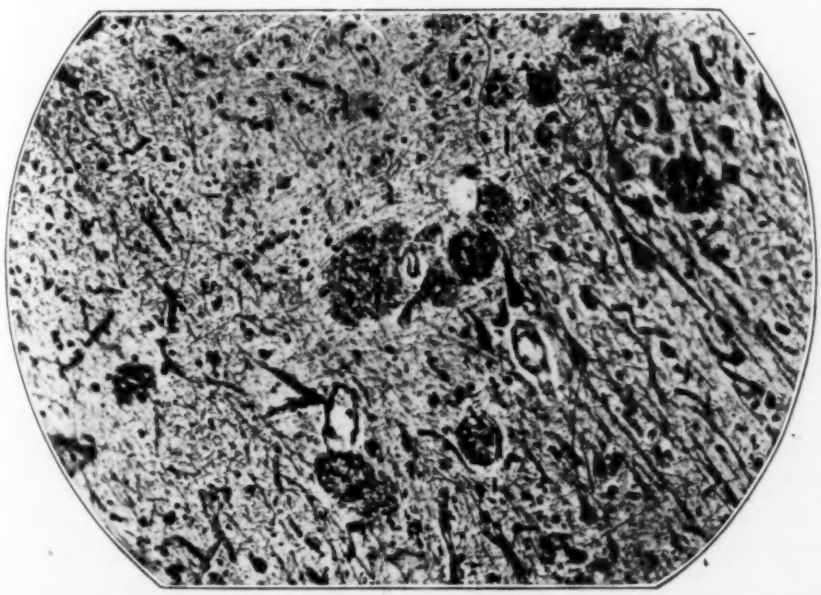

Fig. 3.—Polycyclic, confluent perivascular plaques in Ammon's horn.

observes plaques with a pseudonuclear central mass (fig. 5) but they are rare and isolated. The center is more amorphous, the tint is less argentophile, and the mass looks like an imperfectly made crown, from which large filaments emerge. These masses having a mycelial appearance reproduce the "bulles" described by Ley.[23] They belong to neighboring irritated axons or to neuroglia cells.

The plaques may retract concentrically, revealing the "zone X" of Tumbelaka,[24] but the existence of this pericellular space has been exceptional in our preparations. On two occasions (figs. 7 and 8) we have seen a crystalloid mass, an irregular silver precipitate adherent

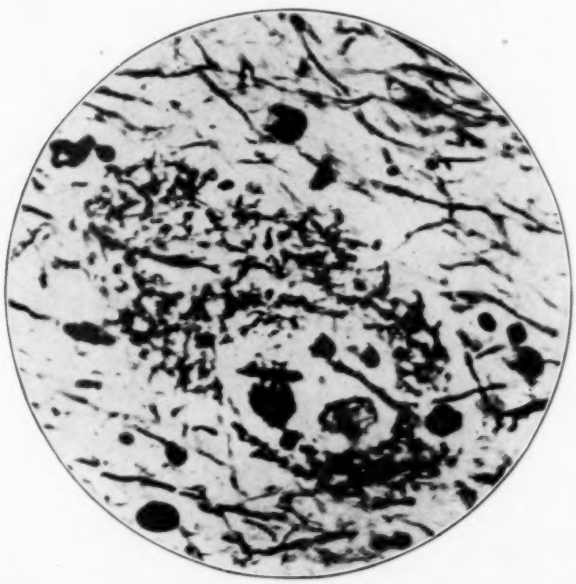

Fig. 4.—Senile plaques with vacuoles and globuloid inclusions.

to the neuroglia cell, superimposed on nerve tissue. They recall the very special formations described by Laignel-Lavastine and Tinel;[25] we have not been able to verify the elective staining properties of fatty acids which they describe.

Such are the forms of senile plaques which we have seen. This is not the place to discuss the origin of senile plaques and the rôle of neuroglia (Alzheimer) or microglia cells (Ley) in their genesis. We shall, however, discuss briefly their evolution. Is the stage of "plaques with pseudonuclear mass" one of preterminal resorption of senile

23. Ley (footnote 8, p. 35).

24. Tumbelaka: Ziekte van Redlich-Alzheimer, Psychiat. en neurol. Bla., 1920.

25. Laignel-Lavastine and Tinel: Deux formes de plaques corticales dans la démence sénile, J. de psychol. norm. et path. **22**:113, 1922.

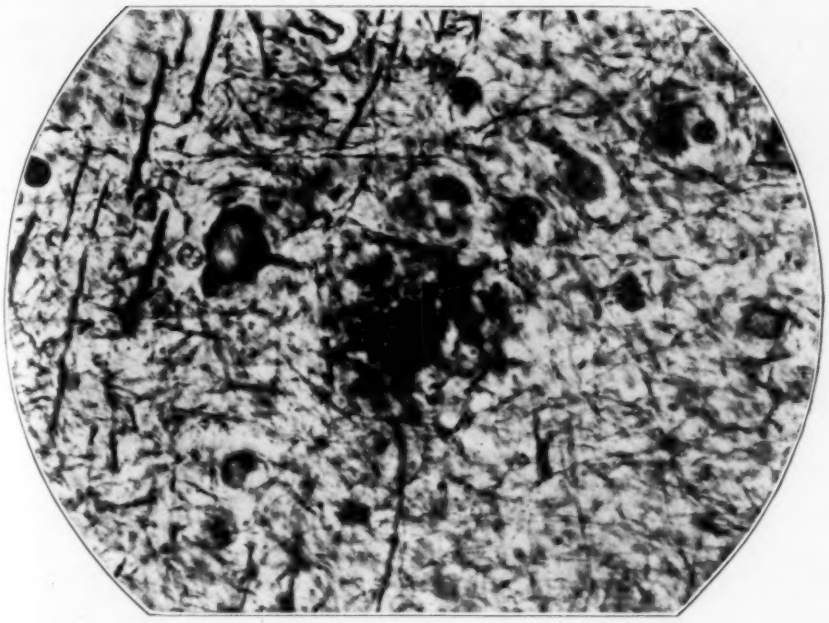

Fig. 5.—Senile plaque containing a pseudonuclear organ.

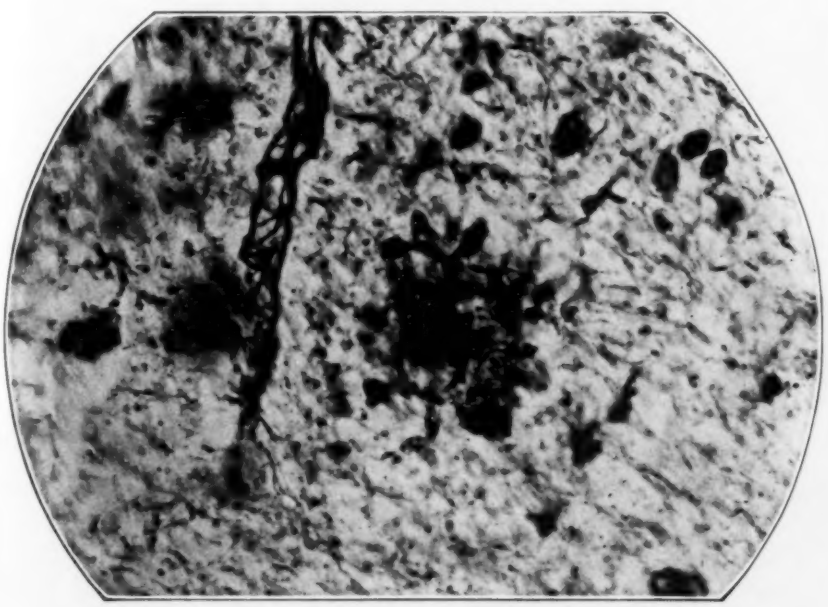

Fig. 6.—Senile plaque containing bulbous filaments at its periphery.

formations preceding their complete disappearance (Tinel), or has the plaque this form because it acts as a center about which microglial elements arrange themselves in crystalloid groups in order to remove it by phagocytosis, a "center of call" whose structure is complicated by the presence of axons, dendrites and neuroglial elements in reflex proliferation (Ley)? Tinel's conception of the problem of the evolution of these plaques from a chemical point of view and from that of the neighboring and concomitant cell and neuroglial lesions was very original:[26] "The initial senile plaque appears as an amorphous sub-

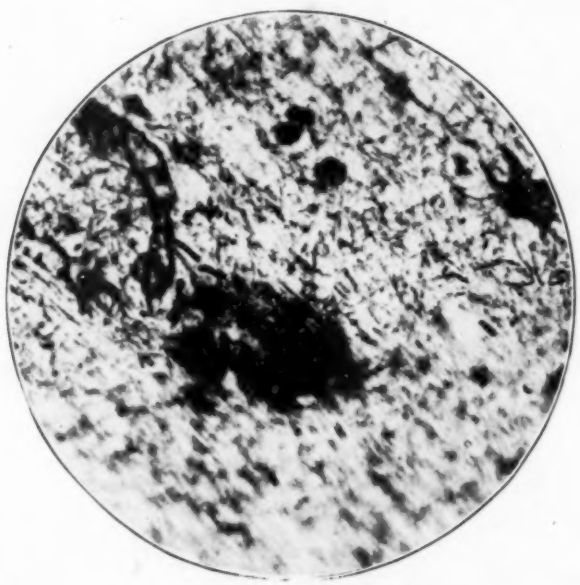

Fig. 7.—Agglutination of an argentophil substance about a neuroglia cell; the crystalloid structure of this mass should be noted.

stance simply superimposed on nervous tissue which does not in the least alter its various constituent elements. At this period there is no neuroglial reaction or nerve lesion. One notes only that the cell and the nerve fibers which cross it are impregnated by an argentophil substance which stains with particular intensity. Senile plaques that have existed for a long time may be recognizable by the neuroglial reaction and the pathologic appearances of cells and fibers, both of which have developed slowly because of the irritating contact of the precipitated substance. This is what one may call the cicatricial stage of the senile plaque.

26. Tinel (footnote 21, pp. 23-25).

"At this point it must be emphasized that two kinds of evolution may obtain according to the location in the cortex. The plaque may evolve in the direction of neuroglial proliferation, or in the direction of cell dystrophy (lesion of Alzheimer) or lesions of nerve fibers."

The question arises whether the neuroglial and ganglionic reactions have a chronologic significance as precise as Tinel believes, and whether they give exact information as to the age and evolution of the plaque. We believe that regenerative reaction of the nerve fibers in contact with the plaques is to be observed at the initial adult and terminal stages of these formations. The neuroglial reaction may exist in sections showing plaques in the process of involution, without in the least sug-

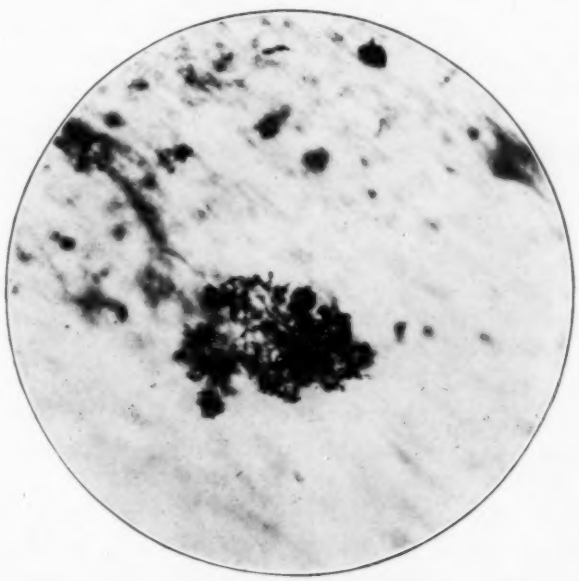

Fig. 8.—The central neuroglia cell in a crystalloid mass.

gesting the idea that this reaction is taking place about these involuting plaques.

Neuroglia, furthermore, may be entirely lacking in the neighborhood of plaques whose structure is exceedingly degenerated. The cellular modification described by Alzheimer is observed as frequently in the neighborhood of young plaques as of those which may be considered adult or very old. They may be entirely absent in the cortex where plaques with pseudonuclear masses are observed, and near to which the cells show only fatty infiltrations. The facts are sometimes too complex to be explained by the ingenious hypothesis of Tinel. It is probable that there is no relation between the crystalized plaques of Laignel-Lavastine and Tinel, the miliary sclerosis of Blocq-Marinesco

and the lesion of Alzheimer—no relation which can be assimilated to the question of evolution of disintegration in plaques. We are of the opinion that a scheme of correlation of these structures like that of Tinel is too rigid.

It is true that we are beginning to understand the factors which play a part in this syndrome of crystalloid irritation which constitutes the senile plaque. But who would dare to indicate the stages of the syndrome, and why not consider that there is a margin of individual variation such as is observed in other progressive biologic phenomena?

THE CELLULAR LESION OF ALZHEIMER

This cell lesion has suffered the same vicissitudes as the senile plaques, and some continue to consider them as strictly identical lesions (Ziveri [27]). At first Kraepelin [28] thought them typical of Alzheimer's disease; subsequently the lesion was described in the various forms of senile dementia (Lhermitte and Nicolas,[29] Lhermitte and Cuel,[30] Cuel [31]) and in normal senility (Fuller,[32] and Ley [33]). Lewy [34] has described it in the basal ganglia and the neighboring gray matter in true Parkinson's disease and has reproduced it experimentally by parathyroidectomy. Schaeffer has observed them in a very young person with hereditary cerebellar ataxia. Before Lewy, Cajal and Tello studied thickening of neurofibrils in hibernating animals; and their researches were completed experimentally by Donnaggio and his pupils.

However, none of these investigations has convinced pathologists, and Frigerio [35] justly observes that in the lesion of Alzheimer two processes occur: (1) agglutination of neurofibrils with characteristic figures; (2) overstaining of the fibrils—this latter change has not been experimentally reproduced. He asks whether these fibrils are really neurofibrils and whether they are not fibrils of connective tissue or glial origin—adherent to the surface of the nerve cells as the result of

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27. Ziveri: Beiträge zur Kenntniss des präsenilen Irreseins, Ztschr. f. d. ges. Neurol. u. Psychiat. **8**:255, 1912.

28. Kraepelin (footnote 10).

29. Lhermitte and Nicolas: Sur la maladie d'Alzheimer, Paris méd. **13**:301 (Oct. 20) 1923.

30. Lhermitte and Cuel, J.: Sur l'anatomie pathologique de la maladie d'Alzheimer, Encéphale **19**, 1924.

31. Cuel, J.: La maladie d'Alzheimer, Thèse de Paris, 1924, p. 83.

32. Fuller (footnote 17, p. 7).

33. Ley (footnote 8, p. 60).

34. Lewy, L. H.: Die Veränderungen des fibrillären und canaliculären Apparates der Ganglienzellen im Senium, Zentralbl. f. d. ges. Neurol. u. Psychiat. **26**:25, 1921.

35. Frigerio, Arrigo: L'anatomia pathol. delle psicosi senili, Prem. Stab. d'Arti graf. Cav. G. Federici, Pesaro, 1923, p. 82.

precipitation. He is, therefore, not far from the view of Simchowicz [36] who asks whether the lesions of Alzheimer are not extracellular agglutinations.

Careful histologic examination shows that, in reality, the condition described by Alzheimer is not manifested in one way alone: 1. Cellular elements or neurofibrils are found with a delicate spiral formation and showing a delicate filigree or producing basket-like formations whose meshwork remains pale and distinct (fig. 9). These cells may be destroyed; then the material forming their delicate structure is spread through the ground substance of the nervous system. 2. There are

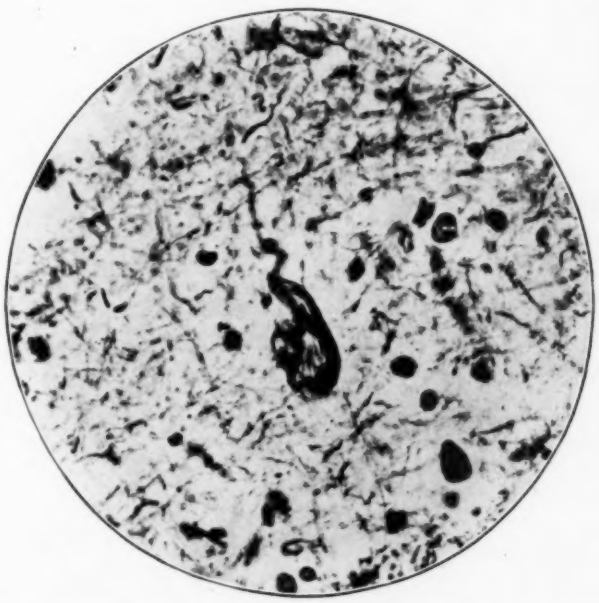

Fig. 9.—A cell showing the lesion of Alzheimer, fine fibrils and hyperchromia.

cells with a thicker filigree, darker, less graceful and duller, rolled up in a knot or taking the form of a figure eight, the cell body being degenerated (fig. 10). As the cells are destroyed they leave a mycelium or pseudofilamentous structure. 3. There are cells that have undergone sclerosis and become thickened, which contain agglutinated masses of neurofibrils having the form of a flame, a comma, a crescent or a triangle (fig. 11). They are hyperchromatic, and when they undergo disintegration leave, in the ground substance of the tissue, opaque silver-stained granules of various shapes, sometimes angular.

These three types of cell dystrophy, most probably three phases of the same process, may be found side by side in our preparations. They

36. Simchowicz (footnote 20, p. 283).

may possibly represent the various stages produced experimentally in animals. Beautiful examples of the lesion of Alzheimer may be found near senile plaques, but they may also be found far from them or even when they are absent (Ley).

THE GRANULOVACUOLAR LESION OF SIMCHOWICZ

This lesion was observed by Alzheimer [37] in the arteriosclerotic brain, but Simchowicz [38] gave it the name it now bears and described it [39] as existing next to the lesion of Alzheimer in the horn of Ammon in cases of senile dementia. It has not been described in any disease

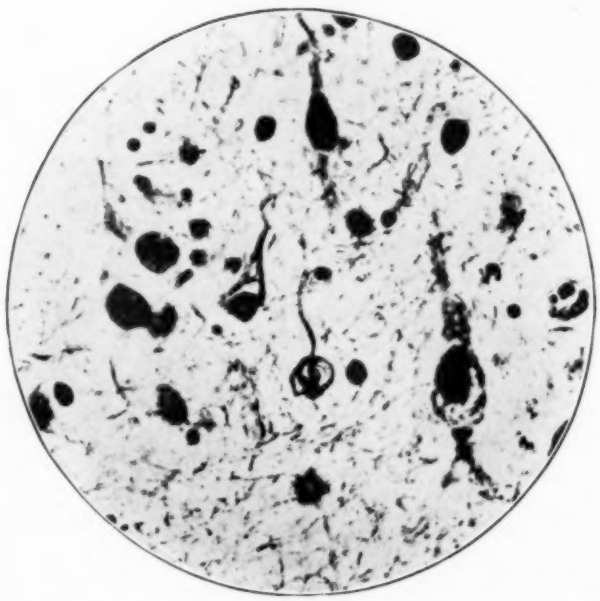

Fig. 10.—Cellular lesion of Alzheimer showing filamentous agglutination of neurofibrils.

other than that of Alzheimer in senile dementia, and Ley [40] remarks that he has not observed it in mentally normal senile persons.

The cell protoplasm shows one or more confluent vacuoles of varying shape, containing granules of various sizes, often isolated. The ideal method for their study is that of Bielschowsky with methylene

37. Alzheimer: Seelenstörungen auf arteriosklerotischen Grundlage, Allg. Ztschr. f. Psychiat. **59**:697, 1902.

38. Simchowicz, T.: Histologische Studien, Histol. u. histopath. Arb. u. die Grosshirnrinde **4**:271, 1911.

39. Simchowicz (footnote 20, p. 223).

40. Ley (footnote 8, p. 61).

blue-eosin. The granule is blue in a cell outline with silver and the vacuole is colorless. Frigerio [41] states that the vacuoles stain entirely or in part with dyes and that the granules take a light blue with thionin. We have used the Bielschowsky stain. The granules are quite black and of all sizes. The protoplasm is clear and the nucleus is pushed to the periphery (fig. 12). The cell as a whole may be sclerosed and the fibrils in its processes may be agglutinated, while the cell body shows the special vacuole degeneration described.

The cell may be represented only by a filiform skeleton filled with silver-staining granules. It may lose its processes and the granules may

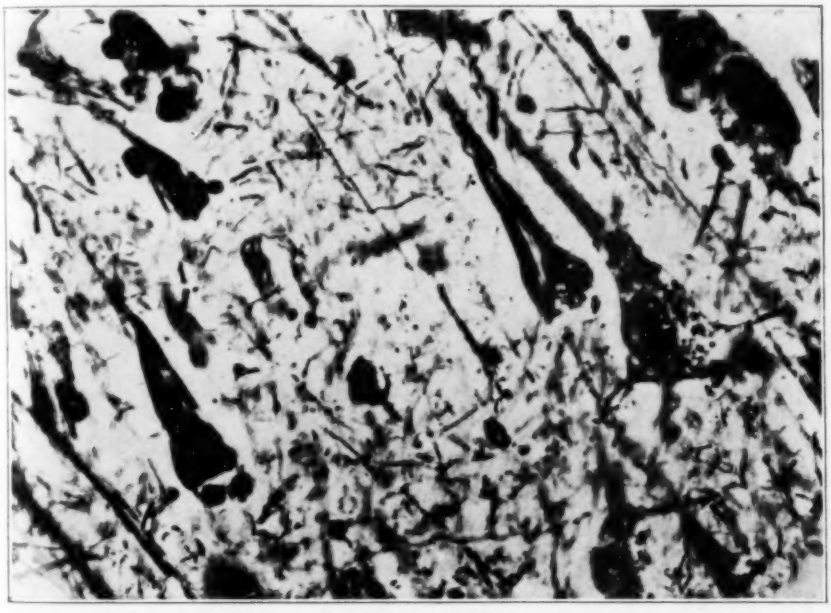

Fig. 11.—Cellular lesion of Alzheimer showing agglutination of fibrils and flamelike hyperchromic retractions.

be dispersed in the ground substances. If they become agglutinated in the region of a destroyed Alzheimer cell, they may present the appearance of a pseudofilamentous senile plaque. As Simchowicz has shown, true granulovascular degeneration is observed only in the pyramidal cells of Ammon's horn, and it is closely allied to the cell lesion of Alzheimer (fig. 13).

OTHER CELLULAR AND NEUROLOGIC LESIONS

We shall lay no emphasis on simple hypochromatic cellular sclerosis, fatty degeneration and the association of the two lesions of this fatty

41. Frigerio (footnote 35).

sclerosis which has been well established by Simchowicz. There is nothing specific in these changes and they may be observed in a great many different diseases. It is not possible to schematize the varieties of neuroglial reaction nor their importance. They may be minimal and limited to proliferation of fibrous glia around the blood vessels of the white matter, and in the white matter adjacent to the gray. They may invade the entire thickness of Ammon's horn up to its first layer, and may contain giant hypertrophic astrocytes showing atypical proliferation. The deep layers show a mixture of fibrous astrocytes and ameboid glioplasmatic cells. The fascia dentata may also be invaded

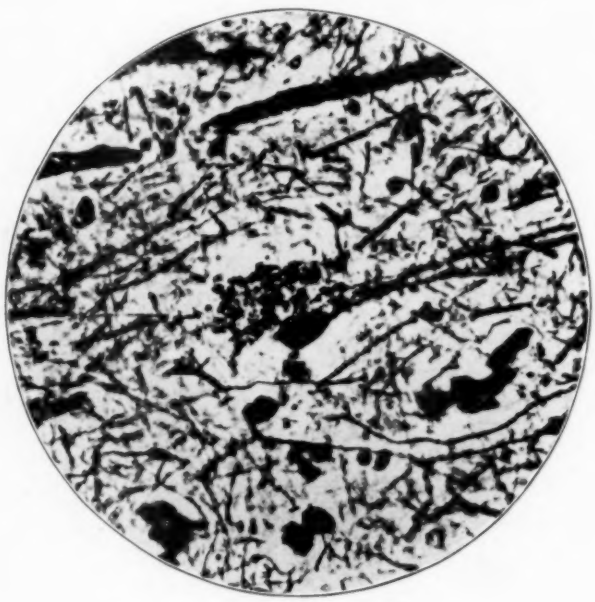

Fig. 12.—Cellular lesion of Simchowicz.

by astrocytes with various peculiar shotlike processes. Because the technic we have used involved long fixation in formaldehyde, we were unable to study the microglia.

L'ÉTAT CRIBLÉ

The two cases we have studied from the point of view of the changes dependent on senility and of the atypical cell lesions which might be present, both showed a lacunar condition about certain blood vessels of the frontal lobe. First observed by Durand-Fardel, Proust and Demange, and described for the first time by Alzheimer in 1898, it is to Pierre Marie and his pupils, Ferrand, André Leri and Catola, that we owe a clear demonstration of the pathologic significance of these

changes and completion of the histologic studies of the disintegration of the lacunae. This lacunar state of Pierre Marie, from a histologic point of view, belongs in the same category as the état précriblé of Vogt. The only difference between them is that the lacunar state is generally seen in the basal ganglia while the état criblé is seen more especially in the centrum ovale and the more myelinated areas generally. According to Bertrand, "The lacunae, therefore, schematically are dilatations of perivascular sheaths associated with rarefactions in the surrounding ground substance." At present, the majority of pathologists subscribe

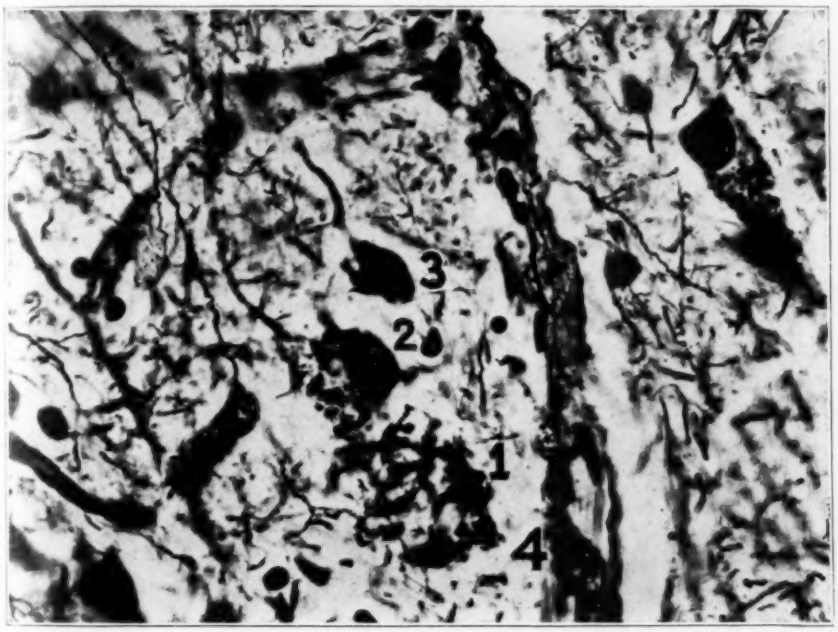

Fig. 13.—The zona hippocampa of Ammon's horn: *1* indicates "pseudomycelium" senile plaque; *2*, cellular lesion of Simchowicz; *3*, cellular lesion of Alzheimer; *4*, argentic over-impregnation of a capillary.

to the opinion of Pierre Marie and Catola that the phenomena of localized perivascular lacunae originate from the same toxic cause as arteriosclerotic lesions.

In lateral sclerosis we found all intermediate stages between capillary sclerosis with scarcely visible rarefactions of the nervous parenchyma—the variety which lies next to the blood vessels and contains no true granular bodies but only amorphous metachromatic substances (fig. 14)—and the true lacunar state. Between the two comes the état criblé (fig. 15) which, at its onset, shows granular bodies and macrophages in the perivascular space and in which, at a more advanced stage, there

float in the adventitial perivascular cavity the filamentous fringes of the old adventitia. These lacunae are easily demonstrated at the border of the transition between white and gray matter. The existence of a similar type of perivascular necrosis is associated with long evolution of the disease. They recall the lesions which have been observed by Levy [42] and Bertrand [43] in epidemic encephalitis. In the prolonged form of epidemic encephalitis there are found all varieties of senile vascular lesions which may or may not be combined with cortical nuclear atrophy. We shall not speak again of the analogy between the processes of disintegration in amyotrophic lateral sclerosis and those seen in

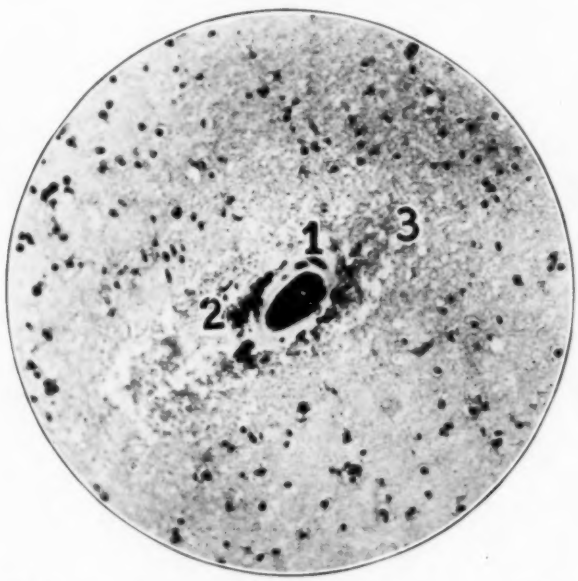

Fig. 14.—Beginning of a premeshlike lesion ("état précriblé"): *1* indicates capillary sclerosis; *2*, deposits of amorphous metachromatic substances; *3*, rarefaction of the juxtavascular parenchyma.

senile sclerosis. The two processes result from closely allied metabolic disorders.

In these conditions the état criblé, précriblé and lacunar state must be regarded as stages of a single process of perivascular parenchymatous disintegration, which may be observed in both toxic and infectious processes, and the common characteristic of which is its development during a prolonged period of time.

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42. Levy, Gabrielle: Les manifestations tardives de l'encéphalite epidémique, Thèse de Paris, 1922, p. 158.

43. Bertrand (footnote 2, p. 120).

CONCLUSIONS

Such typical senile lesions are exceptional in Charcot's disease, twenty-nine cases of which we have investigated.[44] We are unwilling to attempt the establishment of a relation between their presence and the possibilities of mental disorder. This relation we believe to be impossible of solution. An observation exists, however, which we believe to be akin to ours. It concerns a case of lateral sclerosis published by Barrett [45] who states that the presence of argentophile plaques in microscopic examination of the brain compels the admission of a possibility of an unusual Alzheimer's disease.[46] In the cases which we

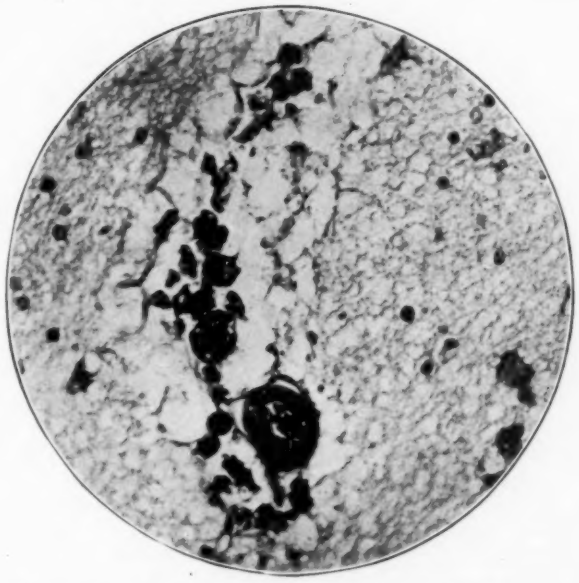

Fig. 15.—"État criblé" (meshlike lesion) in the first frontal convolution (Brodmann's area 8).

report there is no suggestion of the syndrome of Alzheimer but they are none the less interesting from the point of view of neuropathology. Histology begins to free itself from the idea of specific cellular processes; this has even been applied to such specific diseases as

44. Bertrand, Ivan; and Van Bogaert, Ludo: Rapport sur l'anatomie pathologique de la sclérose latérale amyotrophique, Rev. neurol. **32**:779 (June) 1925.

45. Barrett: A Case of Alzheimer's Disease with Unusual Neurological Disturbances, J. Nerv. & Ment. Dis. **40**:361, 1913; quoted by Cuel.

46. Since this paper was written we have found a report of a case of amyotrophic lateral sclerosis with cerebral lesions of the senile type and particularly with senile plaques. Natzdorff, Paul: Zur Pathogenese der amyotropischen Lateralsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:703, 1925.

amaurotic family idiocy and myoclonic epilepsy. We do not concur in this but believe that it should be borne in mind from the point of view of a more general physiopathologic interpretation; it is from this same point of view that disintegrative processes and the specific cellular dystrophies of normal and pathologic senility must be considered.

The presence of these lesions in our cases indicates that the brain, without being beyond the sixth decade, may contain certain pathologic conditions susceptible of causing its involution, when the metabolism of the nervous system approaches that of normal or pathologic senility.

STUDIES ON THE CENTRAL VISUAL SYSTEM

II. A COMPARATIVE STUDY OF THE FORM OF THE GENICULO-STRIATE VISUAL SYSTEM OF MAMMALS *

TRACY JACKSON PUTNAM, M.D.

BOSTON

During the early years of the investigation of the central visual system, much attention was paid to the anatomy and experimental pathology of the visual centers in animals. Von Monakow and his school especially made many studies of the anatomy of the external corpus geniculatum, the tracts of the occipital lobe and the visual cortex. A review of the literature on the experimental aspects of the problem is given by Minkowski,[1] and on the more purely anatomic aspects by Redlich.[2] Interest then shifted more to the study of human pathologic material, and to the finer histology of the cortex. As a result of all these investigations, it is now generally accepted (even by former adherents of the "decentralist" school) that the second neuron of the visual system arises in the corpus geniculatum externum, and ends in the striate cortex (field 17 of Brodmann).[3]

Renewed interest in the comparative anatomic aspect of the subject has been aroused by the work of Brouwer and Zeeman on the projection of the retina on the corpus geniculatum of cats, rabbits [4] and apes,[5] and by the work of van Valkenburg [6] and Minkowski [1] on the projection

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* From the Central Institute for Brain Research, Amsterdam.

1. Minkowski, M.: Experimentelle Untersuchungen über die Beziehungen der Grosshirnrinde und der Netzhaut zu den primären optischen Zentren, besonders zum Corpus geniculatum externum, Arb. a. d. hirnanat. Inst. in Zürich **7**:255-362, 1913; Ueber den Verlauf, die Endigung, und die zentrale Repräsentation von gekreuzten und ungekreuzten Sehnervenfasern bei einigen Säugetieren und beim Menschen, Schweiz. Arch. f. Neurol. u. Psychiat. **6**:201-252, and 269-303, 1920.

2. Redlich, E.: Zur vergleichende Anatomie der Assoziationssysteme des Gehirns der Säugetiere, II, Der Fasciculus longitudinalis inferior, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **12**:108-206, 1905.

3. Brouwer, B.: Ueber die Sehstrahlung des Menschen, Monatschr. f. Psych. u. Neurol. **41**:9-158, and 203-234, 1917.

4. Brouwer, B., and Zeeman, W. P.: Experimentell-anatomische Untersuchungen über die Projektion der Retina auf die primären Opticuszentren, Schweiz. Arch. f. Neurol. u. Psychiat. **13**:118-135, 1923.

5. Brouwer, B., and Zeeman, W. P.: Experimental Anatomical Investigations Concerning the Projection of the Retina on the Primary Optic Centers in Apes, J. Neurol. & Psychopathol. **6**:1-10 (May) 1925.

6. Van Valkenburg, C. T.: Zur Anatomie der Projektions—und Balkenstrahlung des Hinterhauptlappens sowie des Cingulums, Monatschr. f. Psychiat. u. Neurol. **24**:320-339, 1912.

of the corpus geniculatum on the striate cortex. The result of these investigations is, that we now know the general position of the regions of representation of the respective retinal quadrants in the external geniculate body and cortex. In addition, the view of Flechsig [7] that the inferior longitudinal fasciculus, and not the stratum sagittale internum, is the geniculocortical radiation, appears to be gaining ground. A renewed investigation of the normal anatomy of all these structures, therefore, seems advisable.

MATERIALS AND METHODS OF STUDY

All the prepared mammalian brains in the collection of the Central Institute for Brain Research were examined. Complete serial sections of the central visual system, stained for the most part by the Weigert-Pal and van Gieson methods, of the following animals were available: *Didelphys marsupialis, Phascalomys, Macropus giganteus, Macropus robustus, Tamandua tetradactyla, Erinaceus europaeus, Talpa europea, Hypsiprimnus murinus, Canis familiaris* (several specimens), *Phoca vitulina, Lepus cuninculus* (several specimens), *Sus scrofa, Elephas indicus, Phocaena communis, Lemur catta, Cebus capucinus, Cebus fatuellus, Oedipomidas oedipus, Trogylodites niger.* Several birds, reptiles, amphibia and fishes were also examined.

The general size and shape of the external geniculate body, optic radiation and striate cortex were determined in each specimen. Significant variations from the usual conditions were noted, and sketched or photographed. In order to obtain a plastic idea of the shape of the visual system, wax-plate reconstructions were made of the rabbit, cat and monkey (*Cebus fatuellus*), each of these animals being representative of a special type, and being useful experimental objects. The stereoscopic drawings presented herewith were made by means of Berville's "Chambre-claire universelle," with which an absolutely accurate outline can be drawn, as if regarded from a fixed point. Two aspects of each model were sketched with an angle between them of about 10 degrees. The resulting illustrations were found more clear than photographs of the wax models, which are seldom satisfactory.

No fine histologic studies of the corpus geniculatum or cortex were made. For these, the reader may be referred to the works of von Monakow, Cajal, Brodmann, Vogt and others (references given by Kappers [8]).

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7. Flechsig, P.: Weitere Mitteilungen über die Sinnes und Associationscentren der menschlichen Gehirns., Neurol. Centralbl. **14**:1118-1124, 1895; Weitere Mitteilungen über den Strabkranz der menschlichen Grosshirns, ibid. **15**:2-4, 1896.

8. Kappers, C. U. A.: Die vergleichende Anatomie des Nervensystems der Wirbeltiere und des Menschen, II Abschnitt, Haarlem, de Erven F. Bohn, 1921, pp. 946-957.

GENERAL PHYLOGENETIC DEVELOPMENT OF THE CENTRAL VISUAL SYSTEM

The corpus geniculatum externum may be recognized in fishes. It consists of a nest of cells, lying in the angle between the optic tract and the tectum opticum. Fibers enter it from the optic tract and leave it by the medial and lateral brachii tecti laterales, and perhaps a few by the posterior commissure. In some fishes, two groups of cells are seen (Kappers[9]). In amphibia and reptiles, only one cell group is present which sends fibers to the tectum opticum, and also mesially to the thalamus. In birds the mesial fibers may be traced to the "spiriform nucleus." In all these animals the fibers of the optic tract are very coarse. The other fibers arising in the corpus geniculatum are also coarser than most tracts in the vicinity, but not as coarse as the optic tract itself. Further details of the comparative anatomy of the visual system of lower vertebrates may be found in Kappers' book.[10]

In placentalia, with which this paper is chiefly concerned, there is an abrupt change. The corpus geniculatum externum assumes a form which is familiar to us in rabbits, with a ventral and dorsal nucleus. The neuron arising in the corpus geniculatum runs to the newly formed pallium. The cortical visual area is difficult to localize in the lowest members of the group, and the optic radiation is not to be distinguished from the surrounding white matter.

In certain blind, or almost blind, animals (*Talpa europaea*, for example) the visual system is so primitive that we can scarcely speak of a well defined form. Descriptions of the brains of such animals have been published by Ganser [11] and Frankl-Hochwart.[12]

According to Bouman,[13] corticifugal fibers running from the occipital lobe to the geniculate body and anterior colliculus are found in the rabbit. Their anatomic course is not known, however, and they will not be considered further here.

The tractus peduncularis transversus, which also contains fibers from the optic nerve, is of course not included in the geniculostriate system. No especial attention was paid to it, therefore, during this study. It

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9. Kappers, C. U. A.: The Structure of the Teleostian and Selachian Brain, J. Compar. Neurol. **16**:1, 1906.

10. Kappers (footnote 8, pp. 813-817).

11. Ganser, S.: Vergleichend-anatomische Studien über das Gehirn des Maulwurfs, Morphol. Jahrb. **7**:591-725, 1882.

12. Frankl-Hochwart, L.: Zur Kenntnis der Anatomie des Gehirns der Blindmaus, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **8**:190-220, 1902.

13. Bouman, K. H.: Experimentelle onderzoekingen over het cerebrale optische stelsel, Inaug. diss., Amsterdam, 1905.

apparently corresponds to the basal optic tract of birds (Marburg,[14] Kosaka and Hiraiwa [15]).

THE EXTERNAL GENICULATE BODY

A well formed corpus geniculatum of the primitive mammalian type is found in marsupials (fig. 1). It consists of two bean-shaped nuclei lying in the optic tract. The dorsal nucleus is the larger, and it appears from the investigations of Monakow,[16] Brouwer [4] and Putnam and Putnam [17] and others that it alone, and not the ventral nucleus, atrophies after cortical lesions. This conception is supported by the study of *Didelphys marsupialis,* from which figure 1 is taken. It may be seen that there is a heavy bundle of thick fibers radiating mesially from the dorsal nucleus alone. The ventral nucleus atrophies after section of the contralateral optic nerve, but its central connections are unknown. According to Kappers,[8] it is probably homologous with the corpus geniculatum of fishes, reptiles and birds.

The histologic structure of the primitive mammalian type of external geniculate body requires little comment here. It has been well studied by von Monakow,[16] Cajal [18] and others, and pictured by Winkler and Potter.[19] It is made up of small and medium sized cells and contains tufts of coarse fibers. Some of these come from the optic tract; others may be followed vertically through the tract into the thalamus, and are doubtless projection fibers. Further histologic details may be read in the general surveys of Sachs [20] and Neiding,[21] in which the conditions in many different animals are pictured.

There is great variation in the proportion between the ventral and dorsal nuclei in various species. In the common pig, the dorsal nucleus

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14. Marburg, O.: Basale Opticuswurzel und Tractus peduncularis transversus, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **10**:66-80, 1903.

15. Kosaka, K., and Hiraiwa, K.: Zur Anatomie der Sehnervenbahnen und ihrer Zentren, Folia neuro-biol. **9**:367-389, 1915.

16. Monakow, C.: Experimentelle und pathologisch-anatomische Untersuchungen über die Beziehungen der sogenannten Sehsphäre zu den infra-kortikalen Opticuscentren, Arch. f. Psychiat. **14**:699-753, 1883.

17. Putnam, T. J., and Putnam, I. K.: Studies on the Central Visual System, I, The Projection of the Retinal Quadrants on the Striate Cortex of the Rabbit, Arch. Neurol. & Psychiat. **16**:1 (July) 1926.

18. Cajal, Ramón y: Textura del Sistema Nervioso del Hombre y de los Vertebrados, Madrid, **2**:658-669, 1904.

19. Winkler, C., and Potter, A.: An Anatomical Guide to Experimental Researches on the Cat's Brain, Amsterdam, Versluys, 1914.

20. Sachs, B.: Eine vergleichend-anatomische Studie des Thalamus opticus der Säugetiere, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **17**:280-306, 1909.

21. Neiding: Die Kerne des Diencephalon bei einigen Säugetieren, Abhandl. d. k. Preuss. Akad. d. Wissensch., 1911 (Anhang).

Fig. 1.—Portion of midbrain of Didelphys marsupialis, showing the ventral (*N. vent.*) and dorsal (*N. dors.*) nuclei of the corpus geniculatum externum; a stream of coarse, heavily medullated fibers (indicated by arrows) is seen to flow mesially and ventrally from the dorsal nucleus only; these are probably geniculocortical fibers. Weigert-Pal stain. × 8.

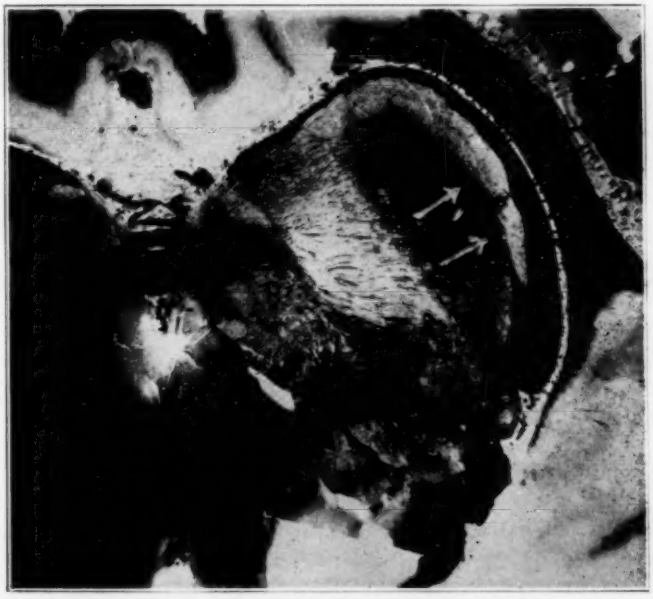

Fig. 2.—Midbrain of Sus scrofa, showing the external geniculate body (indicated by arrows, at the right of the photograph); both dorsal and ventral nuclei are thin and elongated, and are small in comparison with the rest of the brain. Weigert-Pal stain. × 3.

is small and elongated (fig. 2), while in the rat, for instance, it is relatively far larger.[22]

A variation from this primitive condition is seen in cetacea, carnivora, the elephant and the primates in this series. In porpoises and seals (*Phocaena, Phoca*), the corpus geniculatum lies far posterior A ventral nucleus is not to be seen (fig. 3). The geniculate body is slightly concave laterally, instead of mesially as in the primitive type. In *Phoca vitulina,* there is a deep groove on the anterosuperior aspect of the corpus geniculatum, as in land-living carnivora. In these animals we encounter for the first time the row of large cells along the edge of the nucleus

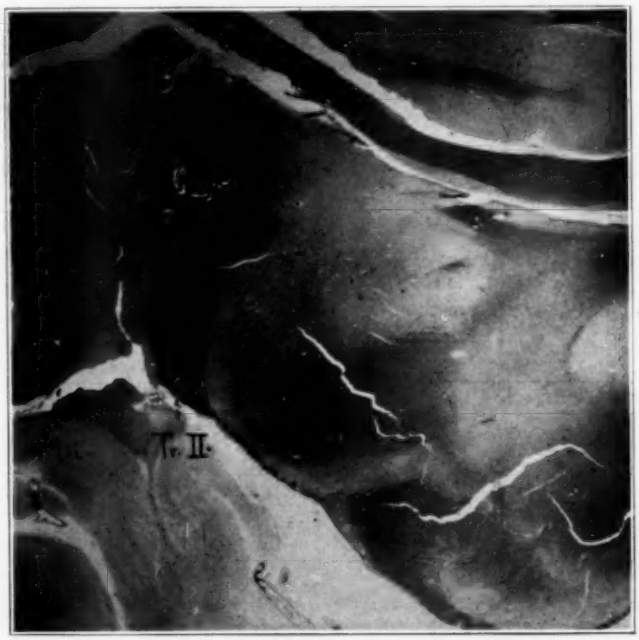

Fig. 3.—Portion of midbrain of Phocaena communis; the optic tract (*Tr. II*) leads upward to the large corpus geniculatum externum (*C. g. e.*); no ventral nucleus is apparent, and the geniculate body lies at the juncture of midbrain and hemisphere; in sections stained by the van Gieson method, a row of large cells is to be seen along its superior and lateral aspect; these, of course, do not show in the present preparation; the dark fibers of the fasciculus longitudinalis inferior (*F. l. i.*) can be seen flowing laterally from the nucleus; it is evident that this is their only origin; certainly they have no connection with the cerebral peduncles (*Ped.*), seen at the bottom of the photograph. Weigert-Pal stain. × 2.

22. Horne-Craigie, E.: An Introduction to the Finer Anatomy of the Central Nervous System Based upon that of the Albino Rat, University of Toronto Press, 1925, plate xviii.

which are such a prominent feature of the corpus geniculatum of the primates. The cells are not as large as in man, and lie irregularly scattered along the superior, lateral and inferior surface. In places, they encroach on the mesial surface also. The corpus geniculatum of the elephant is much like that of *Phocaena* (fig. 4).

The corpus geniculatum of the carnivores may be typified by that of the cat. Its structure is illustrated in detail by Winkler and Potter.[19] It has recently received especial study by Minkowski,[1] and the sections examined for the present paper also showed the presence of a thin row of large cells on the inferior and lateral surface of the nucleus. Definite lamination is present. The shape of the nucleus as a whole is difficult

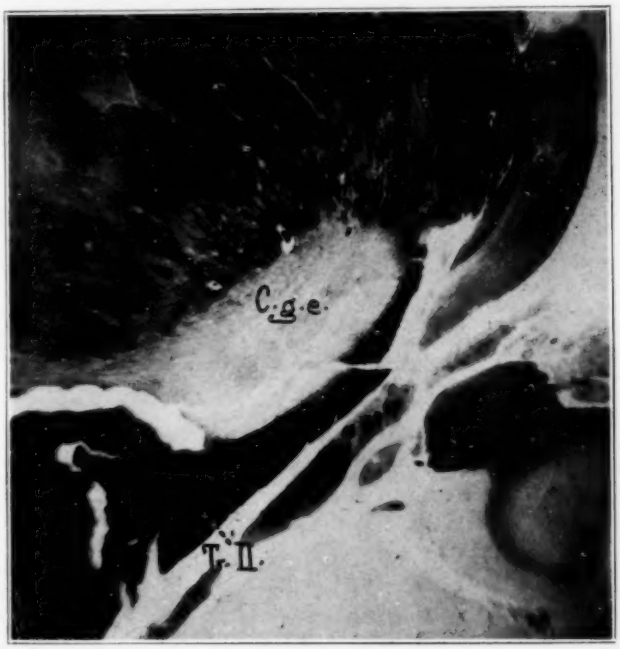

Fig. 4.—Corpus geniculatum externum (*C. g. e.*) of Elephas indicus; no distinct ventral nucleus is seen; projection fibers are difficult to trace. Weigert-Pal stain. × 2.

to describe. It is somewhat reminiscent of a "goose-neck" squash, as the groove seen in *Phoca vitulina* is larger and deeper, and partially cuts off the small dorsal end which bends forward. It is shown in figure 5, but not very plainly, as the groove lies chiefly on the lateral surface. A graphic impression of the shape may be obtained from the illustrations of Overbosch's dissertation.[23] A small ventral nucleus is present. Other details may be read in Sachs' paper.[20]

23. Overbosch: Inaugural dissertation, Amsterdam, to be published.

The corpus geniculatum of the lemur (fig. 6) is in some respects intermediate between that of the carnivora and that of the primates. It is much plumper and larger than that of the cat, and the upper portion is bent backward instead of forward. There is a prominent row of large cells along the lateral surface, and lamination is well marked.

Conditions in the primates are well known. The corpus geniculatum of apes is much like that of man. It is more or less horse-shoe or kidney-shaped, with a definite hilus, at which blood vessels enter, facing downward and mesially. Ordinarily, six distinct layers of cells may be recognized in the macacus, separated by compact sheets of coarse fibers (Minkowski [1]). The large cells are prominent, and lie in two rows along the hilus. Illustrations of the corpora geniculata of other apes are given by Sachs [20] and Friedemann [24] (*Cercopithecus*), and Ziehen [25] (*Tarsus spectrum*).

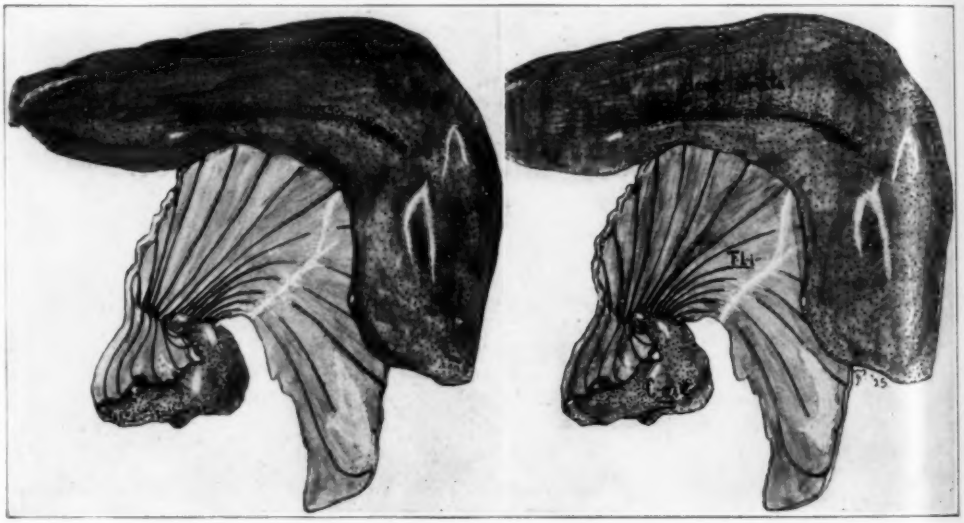

Fig. 5.—Stereoscopic drawings of wax reconstruction of corpus geniculatum externum (*C. g. e.*), fasciculus longitudinalis inferior (*F. l. i.*) and area striata of cat's brain seen from mesial surface; the corpus geniculatum has attained a more complicated form, with a distinct hilus; the beginnings of a "temporal knee" are seen in the optic radiation; of interest is the detour made by the fibers running in the lower edge of the radiation; the area striata appears on the medial as well as the lateral surface of the hemisphere; the indicated direction of the fibers of the radiation is hypothetic. × 3.

24. Friedemann, M.: Die Cytoarchitektonik des Zwischenhirns der Cercopitheken mit besonderer Berücksichtigung des Thalamus opticus, J. f. Psychol. u. Neurol. **18**:37-358, 1911.

25. Ziehen, T.: Einiges über den Faserverlauf im Mittel- und Zwischenhirn von Tarsus spectrum, Monatschr. f. Psychiat. u. Neurol. **14**:1, 1903.

The peripheral position of the large cells in carnivores and primates seems to show that they represent the oldest part of the geniculate body. The geniculate cells arise embryologically from the periventricular matrix, migrating successively in the direction of the optic tract. The primitive condition still persists in the lamprey, where the periventricular cells are in connection with the fibers of the optic tract by means of long dendrites (Kappers). This may be taken as evidence that the large cells are homologous with the ventral nucleus of lower mammals.

Is there any significance in the changes in the relative size, shape and position of the external geniculate body during the course of evolution? There are two landmarks which may aid us to estimate these changes.

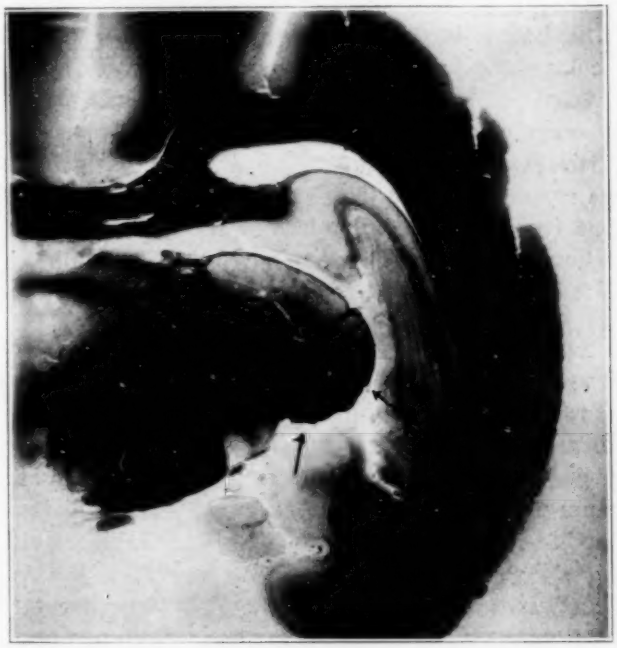

Fig. 6.—Midbrain and hemisphere of Lemur catta; the external geniculate body (indicated by arrows) lies almost horizontally; there is distinct lamination; with appropriate stains, a row of large cells may be seen along its lateral aspect. Weigert-Pal stain. × 3.

One is the position of the binocular field of vision and the macula in the corpus geniculatum, in the animals in which it has been studied (goat, rabbit, cat, ape); the other is the position of the row of large cells, which lie along the surfaces remote from the area of representation of binocular vision in the cat, ape and man.

Thus, in the goat (Minkowski [1]) and rabbit (Minkowski; Brouwer and Zeeman; [4] Overbosch [23]) the area of the binocular vision is small, and

lies on the mesial surface of the dorsal nucleus of the corpus geniculatum. In the cat, the binocular representation is larger, and lies more posteriorly (Minkowski, Overbosch). A small macular area is probably present. The increased binocular area lies at the posteromesial apex of the bow which the corpus geniculatum has made, and it seems conceivable that the deformation has been partly caused by the local increase in volume. The large peripheral cells lie on the anterior and lateral surface. In the lemur, we unfortunately do not know the location of the field of binocular and macular vision, but the large cells lie only on the lateral side. The upper edge of the nucleus has been pushed laterally and posteriorly by the increase in the size of the pulvinar, thalamus and brain stem (Ingvar).[26] This mechanical dislocation has proceeded still further in apes and man, so that the row of large cells has come to lie ventral or slightly ventromedial; and the fields of binocular and macular vision have increased so greatly that they occupy almost the entire nucleus. The result is that the portion of the primate geniculate body corresponding to the top of the geniculate body of the rabbit has come to lie lateral and slightly ventral to the original inferior portion. If we suppose that the blood supply of the primitive mammalian nucleus came from the convex surface of the brain stem, we can then understand how it has come to enter chiefly through the hilus, which is all that is left of it, in apes.

THE OPTIC RADIATION

According to von Monakow and his followers, who have done so much to further our knowledge of the visual system, the geniculocalcarine fibers run chiefly or entirely in the stratum sagittale internum, the pale longitudinal layer of fibers next the ventricular lining. The darker stratum sagittale externum or inferior longitudinal fasciculus has been supposed to contain chiefly association fibers, which could be traced into the temporal and parietal lobes. This opinion was based on experimental degenerations and pathologic cases. The experimental and anatomic work has been criticized by Redlich,[2] and the interpretation of the pathologic cases by Niessl von Mayendorf,[27] who have both come to support Flechsig's view that the entire geniculocortical radiation is contained in the inferior longitudinal fasciculus. A study of the present material leads to the same conclusion, as do the results of anatomic, pathologic and myelinogenetic investigations, which will be published in a later paper.[28]

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26. Ingvar, S.: On Thalamic Evolution, Acta. med. Scandinav. **59**:696-709, 1923.

27. Niessl von Mayendorf: Ueber den Ursprung und Verlauf der basalen Züge des unteren Längsbundels, Arch. f. Psychiat. **61**:273-328, 1919.

28. Putnam, T. J.: Studies on the Central Visual System, III and IV, Arch. Neurol. & Psychiat., to be published.

The reasons for believing that the whole inferior longitudinal fasciculus, and this alone, represents the geniculostriate radiation, may be summarized as follows:

1. In children and young animals, fibers may be traced from the inferior longitudinal fasciculus into the external geniculate body anteriorly, into the calcarine cortex posteriorly and into no other portion of the brain. The internal sagittal layer becomes myelinated at a much later period.

2. In appropriate cases in which there is a large lesion in the vicinity of the corpus geniculatum, but the visual system is left intact, the stratum sagittale internum degenerates, but the inferior longitudinal fasciculus persists unaffected, and can be followed from corpus geniculatum to cortex.

3. Small lesions of the calcarine cortex or of the inferior longitudinal fasciculus produce degenerations which can be traced in this tract into the corpus geniculatum, but which disappear from the stratum sagittale internum as it is followed forward.

4. In animals, the coarse fibers of the inferior longitudinal bundle can be traced into the corpus geniculatum, in which practically no fine fibers such as make up the stratum sagittale internum can be seen. In certain animals (dolphin, seal) the entire longitudinal fasciculus can be seen to arise in the corpus geniculatum, and nowhere else. In other animals (apes) the fibers can be traced into the calcarine cortex, and nowhere else.

5. Following localized lesions of the corpus geniculatum, secondary atrophy is more complete in the fasciculus longitudinalis inferior than in the stratum sagittale internum. This is reported to be true also after long-standing blindness; but evidence is conflicting on this point.

To these direct arguments may be added an indirect one:

6. The inferior longitudinal fasciculus has a characteristic histology, which is like that of the optic tract, the great motor and sensory radiations and the acoustic radiation. No proved association system contains such coarse fibers, but we should expect to find them in an important projection system.

THE INFERIOR LONGITUDINAL FASCICULUS

The inferior longitudinal fasciculus can be studied satisfactorily only in properly stained sections. The ideal stain appears to be that of Weigert-Pal, bleached rather light, and not too blue. Sometimes the coarse fibers stand out very clearly with van Gieson's stain. A general description of the tract has been given by Redlich [2] who has illustrated sections from a large series of animals. This author embarked on his

study as part of his work on the association systems, but came to the conclusion that the tract in question was actually a projection system and did not contain association fibers after all. Exception must be taken to his statement that the most ventral border of the inferior longitudinal fasciculus runs to the hippocampus. Study of the present material makes this seem very improbable, and in the cases of *Phoca vitulina* and *Phocaena communis,* at least, it may be stated definitely that all the fibers of the tract in question arise from the geniculate body (fig. 3). This appears to be the case in the elephant also (fig. 4).

Attention may be called again to the appearance of the fibers first emphasized by Sachs. In favorable sections, the myelin sheath may be seen as a little black ring. Sometimes when the sheath is seen lying in

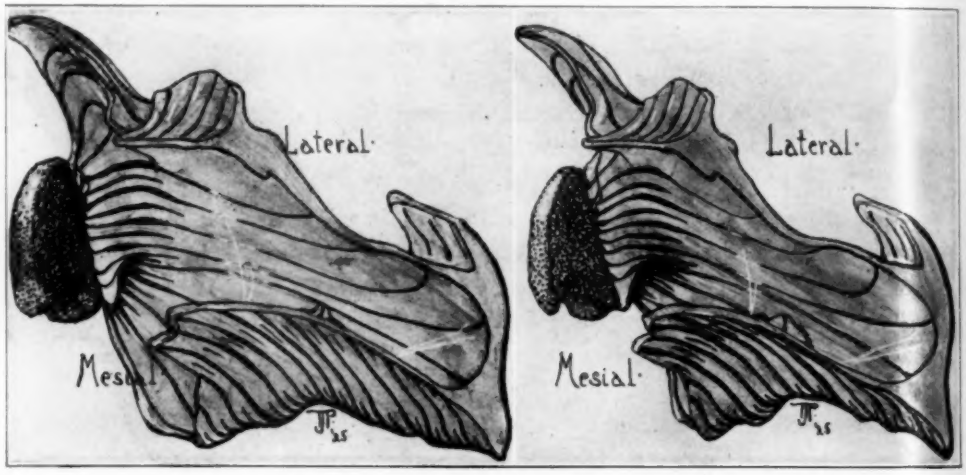

Fig. 7.—Corpus geniculatum and fasciculus longitudinalis inferior of the same model, viewed from behind and mesially; the hilus of the corpus geniculatum is evident; there is some indication that the fibers from the inferior portion of the radiation supply the lateral limb of the corpus geniculatum, those from the upper portion, the mesial limb. × 3.

the plane of the section it appears twisted or wrinkled, as if it were too long for its fiber. Actual spirals are sometimes seen. Then coarse fibers may be traced into the cortex, as far as the stripe of Gennari. This is best seen in carnivora, and is illustrated in Winkler and Potter's atlas of the cat's brain.[19]

The form of the radiation is chiefly of interest in the ape, where it resembles that of man. From figure 7 it can be seen that, proceeding posteriorly from the corpus geniculatum, a stream of fibers is given off from either end of the fasciculus longitudinalis, one below the calcarine fissure, one above. These then turn posteriorly, and run in the longi-

tudinal axis of the brain until the striate cortex appears. They then turn again and run tangentially to the cross-section of the fissure, forming the subcortical white matter. They thus follow a course similar to that of the "bayonet-fibers" of the corpus callosum. The termination of the optic radiation fibers is still more beautifully seen in myelogenetic preparations, as will be described in a later paper.[28]

In appropriate sections it can be seen that fibers are given off from the two ends of the radiation only. Of course, they might be streaming from the middle portion over the ends, but there is no evidence of this. The fasciculus longitudinalis remains of the same thickness throughout its course, but gets progressively narrower from above downward as it approaches the occipital pole (fig. 8). This appears to

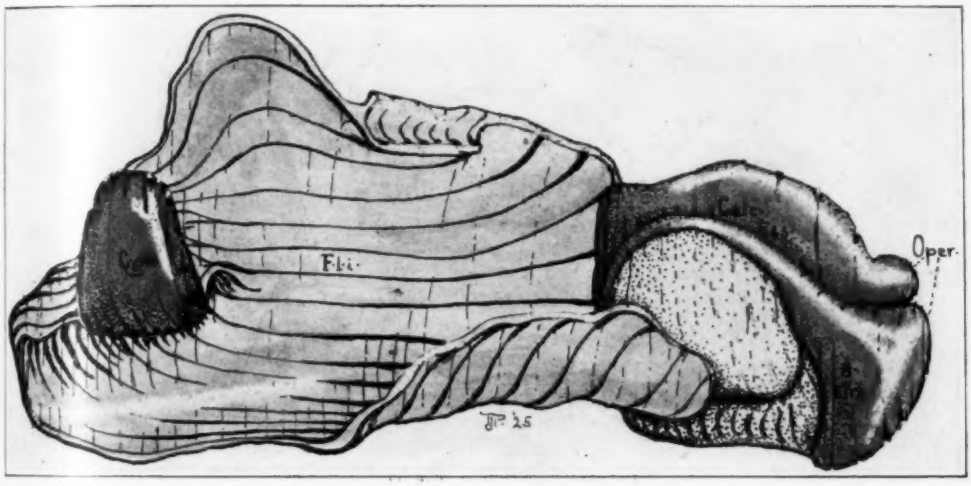

Fig. 8.—General view of the assembled model of the corpus geniculatum externum (*C. g. e.*), fasciculus longitudinalis inferior (*F. l. i.*) and area striata (*A. stri.*) of an ape, Cebus fatuellus; the reconstruction is viewed from the mesial aspect; a distinct "temporal knee" is present, representing a detour of the ventral fibers of the radiation; the most dorsal fibers also make a detour. The height of the compact portion of the radiation begins to decrease before the level of the area striata is reached because of a diffusion of the fibers through the white matter of the occipital lobe; the direction of the fibers of the optic radiation is inferred from the apparent condition in the human brain, which agrees with the necessities of the model. × 3.5.

be a confirmation of the "vertical division" of the optic radiation, which has long been maintained by Henschen for the human subject, and has recently been demonstrated experimentally in the monkey, according to Minkowski.[29] Fibers are given off simultaneously to the mesial and to the lateral cortex at each level. This may be significant, inasmuch as

29. Minkowski, M.: Étude sur les connexions anatomiques des circonvolutions rolandiques, pariétales et frontales, Schweiz. Arch. f. Neurol. u. Psychiat. **15**:97, 1924.

the striate cortex on the lateral surface of the ape's brain is doubtless homologous with the posterior end of the human brain, and here the macula appears to be represented.

A distinct "temporal knee" of the optic radiation is seen in carnivora and primates. In rabbits (fig. 9) and cats (fig. 5) the entire radiation undergoes a rotation through an arc of about 180 degrees, so that dorsal in the corpus geniculatum is ventral in the cortex. In the rabbit (and probably also in the cat) the binocular field of vision is represented

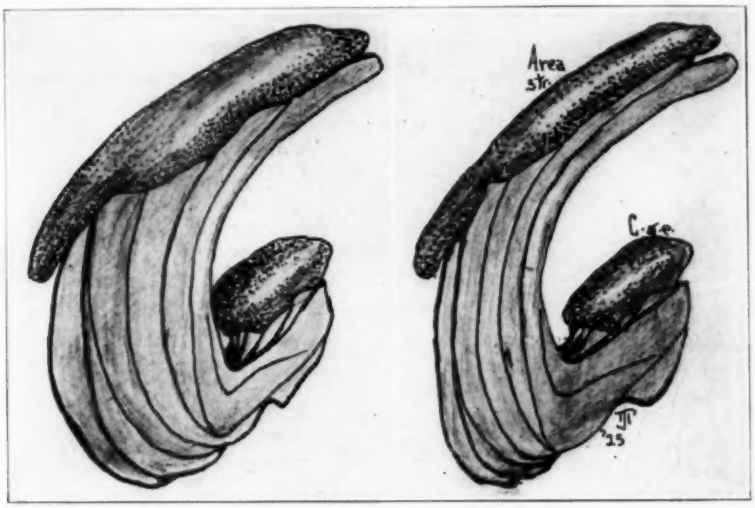

Fig. 9.—Stereoscopic drawings of a wax-plate reconstruction of the corpus geniculatum externum (*C. g. e.*), fasciculus longitudinalis inferior, and area striata (*Area str.*) of a rabbit, Lepus cuninculus; the reconstruction is viewed from its anterolateral aspect; the fibers of the optic radiation bend slightly forward on leaving the ganglion; there is also a slight rotation of the "stalk" of the radiation; the direction of the fibers of the optic radiation is inferred from the work of Putnam and Putnam. (A description of the technic of stereoscopic drawings is given in the text.) × 5.

anteriorly in the radiation (Putnam and Putnam [17]). In man, and probably in apes, it is represented in the middle portion of the radiation, and the monocular fields along the upper and lower edges. This point will be dealt with more fully in a subsequent paper.

DECUSSATING FIBERS

The existence of callosal fibers uniting the corpus geniculatum with the opposite cortex has been postulated on hypothetic grounds by Heine, and Pfeifer [30] believes that he has seen such fibers in myelinogenetic

30. Pfeifer, R. A.: Myelogenetisch-anatomische Untersuchungen über den centralen Abschnitt der Sehbahn, Monogr. a. d. Ges. d. Neurol. u. Psychiat. **43**: 146, 1925.

preparations. His illustrations are not convincing, however, and van Valkenburg [6] has produced important evidence that they do not exist. Reference to other articles on the subject are given in his paper. In some of the animals studied, the corpus callosum, as well as the optic radiation, has a distinctive histology, but no connection could be seen between the two.

THE CALCARINE CORTEX

The shape, extent and histology of the area striata in many animals is well known from the work of Campbell,[31] Brodmann, the Vogts and others, and need not be further discussed here. The area striata is round or oval in marsupials and lower rodents, and gradually acquires a more complicated structure and more definite outline as the phylogenetic

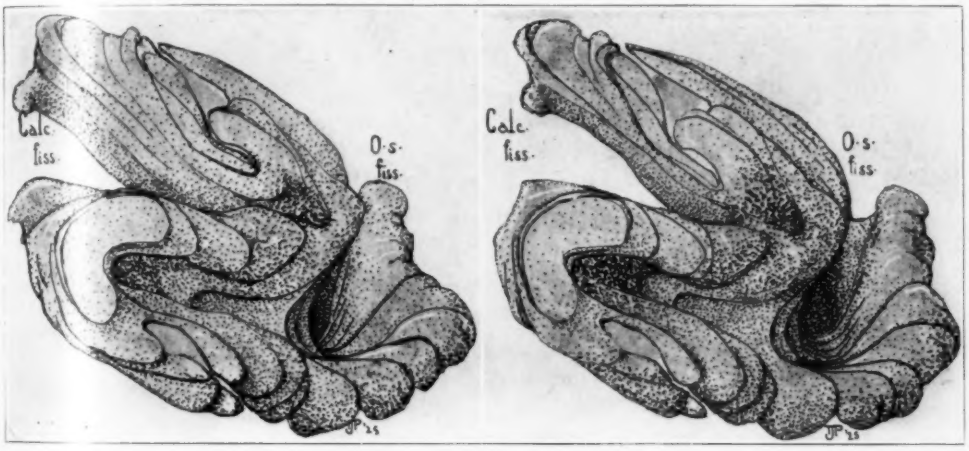

Fig. 10.—The area striata of the same model, viewed from behind; the visual cortex is about equally distributed in the calcarine fissure (*Calc. fiss.*) and occipital superior fissure (*O. s. fiss.*); only a small proportion lies on the surface. × 4.

scale is ascended. It has been suggested in a previous paper that the slight elongation which extends forward from the area striata of the rabbit, and which contains the projection of the binocular field of vision, arose as a result of the differentiation of the new function.

In carnivora, the area striata is about equally divided between the mesial and the lateral surface of the hemisphere, covering also the superior edge of the occipital lobes. In most apes it is also divided between the lateral and mesial surface of the occipital lobes, but includes the occipital pole rather than the upper surface of the hemisphere. There seems to be a distinct tendency for the striate area to sink into the

31. Campbell, A. W.: The Localization of Cerebral Functions, Cambridge University Press, 1905.

depths of fissures and sulci (especially, of course, the calcarine fissure) and for its boundaries to lie on the surface. This is most marked in the primates (fig. 10).

SUMMARY

1. The primitive mammalian type of corpus geniculatum externum, with a dorsal and ventral nucleus, without lamination, lying vertically on the surface of the brain stem is seen in marsupials and lower mammals.

2. Only the dorsal nucleus has a projection on the cortex. An indication of this is seen in the brain of the didelph.

3. Of the animals studied, the cetacea, carnivora and primates showed a variation from the primitive mammalian type of corpus geniculatum. This consists of the almost complete disappearance of the ventral nucleus; the appearance of one or two rows of large cells along the periphery of the persisting dorsal nucleus; certain deformations of the primitive form, perhaps resulting from an increase in the size of the area of representation of binocular and macular vision; and a rotation lateralward, so that the original external surface lies ventrally. The point at which the blood vessels enter the hilus in primates perhaps represents the external (free) surface in lower mammals.

4. In all the animals studied, the fasciculus longitudinalis inferior appeared to be the only system connecting the external geniculate body with the cortex. Its coarse fibers may be seen in the geniculate body. In some animals (*Phoca, Phocaena*) the entire fasciculus can be unmistakably traced to it. The fibers may be traced into the cortex in many specimens.

5. With the other reasons for believing that the inferior longitudinal fasciculus is the geniculostriate radiation should be considered that its fibers resemble those of the optic tract, and also other important radiations. Such coarse fibers are not seen in association systems.

6. In the ape, fibers are given off only from the superior and inferior edges of the longitudinal fasciculus and simultaneously to the lateral and mesial cortex. This speaks in favor of the "vertical division" of the optic radiation. The fibers follow a "bayonet" course to the cortex.

7. No evidence of decussating cortical fibers has been found in the present study.

THE ABORTIVE TYPE OF FRIEDREICH'S DISEASE*

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NEW YORK

The symptom-complex called Friedreich's ataxia was first described by Friedreich of Heidelberg, in 1863. The author at that time, guided only by clinical criteria, supposed the condition to be a juvenile form of tabes dorsalis, being led to this conclusion chiefly by the ataxia and the loss of the knee jerks. However, he emphasized its congenital origin, and recognized the characteristic fact that it showed a remarkable tendency to appear in families. The disease was further studied in 1877 by Schultze who, by means of pathologic examination, recognized the true character of the disease and its essential dissimilarity from tabes dorsalis—that it was a disease entity *sui generis,* with no pathologic relationship to locomotor ataxia. He it was who placed the disease on an independent foundation. His article published in 1877 contains a most satisfactory pathologic description of the gross and microscopic appearances found in the central nervous system of patients dying from Friedreich's ataxia.

During the years since its initial recognition, Friedreich's ataxia has received a considerable degree of attention, having been studied and described by Blocq and Marinesco, Nonne and Mendel, Mingazzini and many others. The clinical history usually elicited from patients suffering from this disease has become familiar and the hereditary features have been firmly established. The physical findings are usually clear-cut and definite and the entire clinical picture has been placed on a sound and satisfactory foundation by the wealth of observations which have been recorded.

It is unnecessary here to enter a discussion of the symptoms characteristic of the disease, and no attempt will be made to describe the pathologic change underlying the clinical manifestations of disordered function. The object of this brief communication is to give the record of three generations of a family in all of which can be found individuals who at varying times of life manifested a group of symptoms and physical signs that constitute a forme fruste of the entire syndrome of "hereditary ataxia." This group of symptoms is limited to the lower extremities and constitutes what may be termed an abortive type of circumferential spinal sclerosis or Friedreich's ataxia.

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* Read at a meeting of the New York Neurological Society, Nov. 10, 1925.

A careful review of the chief textbooks and books of reference has been made in connection with the group of cases to be reported, and either no attention has been given or only the merest mention made of an abortive type of this disease. Oppenheim, in the fifth edition of his textbook of nervous disease, states that abortive forms may undoubtedly occur but presents no description of this type and advances no instances as observed by himself. Lewandowsky's "Handbuch der Neurologie," in its fairly extensive discussion of this condition, makes no mention whatever of any abortive type. Prof. G. Mingazzini, in an article contributed to the *Journal of Mental Pathology* in 1904, reported two cases of Friedreich's ataxia and one case of "so-called abortive form of Friedreich's Disease." This patient presented an ataxia, slight scoliosis, reduction in the patellar reflexes, nystagmoid movements and mental defect developing rapidly and coming on after some sort of acute febrile disease. No mention was made of any stationary period and it is difficult to understand why this patient was considered to present an abortive form instead of an incompletely developed picture of the disease. Marie indicates the variations which may occur in the development of the complete picture of circumferential spinal degeneration by stating that "every patient may have Friedreich's Disease in his own way." Paglieri refers to a "forme fruste" of Friedreich's disease in an article contributed to Tommasi, Napoli, in 1907.

The paucity of evidence as to the possibility of an incomplete or abortive development of this disease justifies the recording of the clinical features characterizing its appearance in this family. The privilege of presenting these patients is due to the courtesy of Dr. Russell A. Hibbs, surgical director of the New York Orthopedic Hospital, to which hospital a number of members of this family went for relief from the locomotor difficulties attendant on the pes cavus.

The family consists of three generations which we have been able to investigate. The passage of time and the birth of later children may supply us with further material. The mother, who presents the most complete development of this abortive incidence of the disease, is (fig. 1) the progenitor of fifteen children. Of these the first, second, third, eighth and tenth are dead; the first child died at the age of 3 months from diphtheria, the second at the age of 10 months from pneumonia, the third at the same age and from the same disease, the eighth at the age of 17 years from tuberculosis and the tenth at the age of 5 months from pneumonia. Ten children of the second generation are living. Of these the first, sixth, seventh, ninth and tenth present evidences of the disease. In the third generation there are six children. The children of the oldest member of the second generation, himself affected by the disease, both show symptoms of the disturbance, as indi-

cated in the table, but the children of the second and third members of the second generation, themselves not involved by the process, have not yet manifested any indication of spinal cord degeneration.

The disease as traced through the three generations has shown the tendency, which is so common in hereditary disease, to appear at a relatively earlier period in each succeeding generation. This anticipating or antedating tendency also appears in connection with the age at which the disease appears in the successive members of the same generation. The disease appeared at the age of 17 in the mother, while in the first living member of the second generation, a boy, it appeared when he was 15, in the sixth member at the age of 12, and in the seventh, ninth and tenth at the age of 10; and in the third generation it appeared at the age of 5 and 4, respectively.

The disease after its onset apparently progresses for a period of from about five to ten years in the various members of this family, and then comes to a spontaneous termination. In the mother this inter-

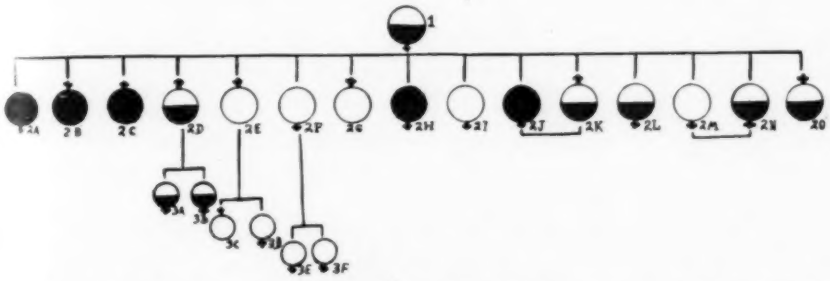

Fig. 1.—Familial record of Friedreich's ataxia: white circle indicates unaffected; black, dead; black and white, affected members of the family.

mission has lasted over a period of thirty-two years, a sufficient time to remove it from the category of a remission, and it seems that it can safely be termed a spontaneous termination. In the members of the second generation, the first showed the signs of the disease at 15; it progressed for five years and then entered a stationary period, which has lasted about thirteen years. The next four living members of the second generation are not affected by the disease. The sixth member, a boy of 19, manifested the onset of this condition at the age of 12 and is now in a stationary period which has lasted for about five years. The seventh member of the second generation, now 18 years of age, showed signs of the degeneration at the age of 10. The condition progressed for about six and one-half years and has remained stationary during the last eighteen months. The eighth child is free from symptoms. The ninth child, now 15 years of age, first showed symptoms at the age of 10; they rapidly progressed for four years and have now been unprogressive for about one year. The tenth

member, the youngest of the family, now aged 12 years, has been suffering from an increasing disability for about two years, and both he and his mother believe that his disability is still increasing.

The first two members of the third generation, the only affected children to date of an affected member of the second generation, are 6 and 4 years of age; in the older the condition has been existent for about one year, while in the younger it was discovered only recently, and in both the condition seems to be progressing. The children of the second and third members of the second generation, themselves unaffected by the disease, show no indication of its appearance. The remaining members of the family have not yet married.

In establishing the chronology of this affection, it has been necessary to date the appearance of symptoms from the earliest noticed difficulty with the feet, as this is the only symptom which has caused these patients any difficulty and resulted in their seeking relief and thus coming under observation. In the young children of the third generation, however, the foot deformity is as yet very scantily developed and the other symptoms, the loss of the patellar and Achilles reflexes and the development of an abnormal reaction of the big toe to plantar stimulation, are also only beginning to appear. Although this fact may not be conclusive proof, yet it may be advanced as tentative corroboration of the assumption that the appearance of the foot deformity is approximately as early as the reflex change.

The group of physical divarications from the normal which constitute this abortive type of peripheral spinal degeneration consist of the typical Friedreich picture confined to the lower extremity, namely, the pes cavus, the diminution or loss of the deep tendon reflexes of the patella and Achilles tendon and an alteration in the response elicited by scraping the outer border of the sole of the foot. In the older members of this group the patellar reflexes have been lost, while in the youngest members the reflexes are sluggish and are apparently diminishing. The grandmother shows a well marked Babinski sign, but the remainder show only a fanning reaction on plantar stimulation. They all show a structural change in the foot, the grandmother showing an extreme pes cavus, the second generation a well marked increase in the arch and the grandchildren the incipient stage of this deformity. The failure of all except one of the members of this group to show any ataxia in the lower extremities is an interesting phenomenon. The oldest son does show a somewhat clumsy gait, but no real ataxia is present.

The anatomic arrangement of the fibers that are supposed to convey the stimuli to the cerebellum and enable that organ to exert its coordinative and synergic control over the lower extremities supplies us

with a very satisfactory explanation for the failure of this symptom to appear. The direct and indirect spinocerebellar tracts, the tracts of Flechsig and Gowers, arise from the cells of Clarke's column and other more loosely arranged cellular accumulations at the base of the dorsal horn. These cell accumulations begin to appear at the second lumbar segment and continue upward through the thoracic and lower cervical segments. There are no demonstrable spinocerebellar tracts below the second lumbar segment. The fibers which complement the spinocerebellar neurons appear from the nucleus of Goll as the dorsal and ventral, internal and external arcuate fibers and gain their entrance into the cerebellum by means of the inferior cerebellar peduncle. There are, therefore, no fibers situated on the periphery of the lumbar portion of the spinal cord conveying deep proprioceptive afferent impulses to the cerebellum in the interest of coordinative and synergic control over the lower extremities. As a consequence this limited morbid process, extending no further upward in the spinal cord than the lumbar segments, exerts no disintegrating influence over the coordinated movements of the lower extremities, and no ataxia appears in the symptom picture.

No sex-linking characteristics of this heredodegeneration are apparent. The first person to be so affected is a female member of the first generation. Her son apparently inherited the disease from her, shows indications of its presence in his own nervous system, and has transmitted it to his offspring. He has three sons who show manifestations of this disease and one son who is not affected. The mother has three daughters unaffected and two involved by the process. In the members of the third generation, we find two female children showing evidences of the disease, having received their taint through an affected father; while a boy and a girl, aged 5 and 3, of an unaffected father, and two girls, aged 5 and 3, of an unaffected mother, are free from the disease. The mortality in the family does not appear particularly significant. There have been five deaths: one from diphtheria, three from pneumonia and one from tuberculosis. The most one can say is that the family has shown itself to be vulnerable to infection.

The physical characteristics of these persons do not supply us with any data of material interest. All members of the family are typical Italians. The father and mother are rather heavily built, elderly people, both with brown eyes, the mother having had dark brown hair. All except two of the children are slight, black-haired and brown-eyed; the two exceptions present chestnut hair and both are free from stigmas of this disease. The affected children of the second generation are somewhat lighter in coloring than their parents. The mother of the affected third generation has dark hair and blue eyes. These facts convey no information of value.

In the second generation, there are two sets of twins. The older set comprises one of the dead children, the tenth child, who died from pneumonia at the age of 5 months, and the sixth living member, who is affected by the disease. The second set, both of whom are living, are dissimilar: one, unaffected, has chestnut hair and a lighter complexion than her affected twin, who conforms with the predominant dark familial coloration.

Careful examination of roentgenograms of the lumbar region fails to disclose any indication of incomplete union which would produce a dorsal or ventral spina bifida. No bony abnormalities could be made out.

The following brief case report of the individuals forming this family is of interest.

Abortive Type of Friedreich's Ataxia

Case	Age	Age at Onset	Course	Ataxia	Gait	Patellar Reflex	Achilles Reflex	Babinski Sign	Fanning Sign	Sensation	Nystagmus	Speech	Pes Cavus	Scoliosis	Coloring
1	57	17	St	0	N	0	0	+	+	N	0	N	+	0	LB
2A	Died at age of 3 months, diphtheria														
2B	Died at age of 10 months, pneumonia														
2C	Died at age of 10 months, pneumonia														
2D	33	15	St	0	?	0	0	0	+	N	0	N	+	0	DB
2E	30	..	..	0	N	N	N	0	0	N	0	N	0	0	DB
2F	28	..	..	0	N	N	N	0	0	N	0	N	0	0	LB
2G	25	..	..	0	N	N	N	0	0	N	0	N	0	0	DB
2H	Died at age of 17 years, tuberculosis														
2I	22	..	..	0	N	N	N	0	0	N	0	N	0	0	DB
2J	Died at age of 5 months, pneumonia														
2K	19	12	St	0	N	0	0	0	+	N	0	N	+	0	DB
2L	18	10	St	0	N	0	0	0	+	N	0	N	+	0	DB
2M	15	..	..	0	N	N	N	0	0	N	0	N	0	0	LB
2N	15	10	St	0	N	0	0	0	+	N	0	N	+	0	DB
2O	12	10	Pr	0	N	0	0	0	+	N	0	N	+	0	DB
3A	6	5	Pr	0	N	++	++	0	+	N	0	N	+	0	LB
3B	4	4	Pr	0	N	++	++	+	+	N	0	N	+	0	DB
3C	5	..	..	0	N	N	N	0	0	N	0	N	0	0	...
3D	3	..	..	0	N	N	N	0	0	N	0	N	0	0	...
3E	5	..	..	0	N	N	N	0	0	N	0	N	0	0	...
3F	3	..	..	0	N	N	N	0	0	N	0	N	0	0	...

N indicates normal; St, stationary; Pr, progressive; LB, light brown; DB, dark brown; 1, first generation; 2A, second generation; 3A, third generation.

REPORT OF CASES

Case 1.—The mother, aged 57, of a family of fifteen children, five of whom are dead, began to complain of trouble with her feet at about the age of 17. This consisted of pain and difficulty in walking, with a certain amount of disturbed control of the feet. The condition progressed until she was about 20 or 25 years of age and has remained stationary since that time.

On physical examination no abnormalities were found in the cardiovascular, respiratory, genito-urinary or gastro-intestinal systems. She presented a moderate degree of round back but there was no lateral deviation or scoliosis. No Romberg sign was present. The gait showed marked interference on account of the extreme deformity of the feet, which presented a marked degree of pes

cavus with extreme rigidity of the foot and immense callosities. Except for this deformity and its interference with gait the patient presented a normal muscle balance and no other abnormalities. No incoordination or ataxia was present. Examination of the reflexes showed an absence of the patellar and the Achilles reflexes. A bilateral Babinski sign was present. The cranial nerves were essentially normal. There was no nystagmus. The pupils reacted to light and in accommodation; speech was normal.

CASE 2.—A man, aged 33, the oldest living member of the second generation, is the father of two children, each of whom shows the beginning of definite disturbance. The disease in his case made its appearance at the age of 15, when the parents noticed a beginning deformity of the feet. This progressed until he was about 20, since which time it has remained essentially stationary. Physical examination shows no defect in the extraneural systems. He shows no scoliosis and there is no definite interference with muscle strength in either the upper or the

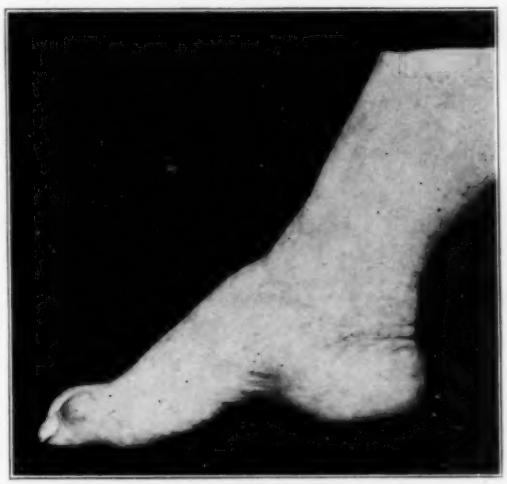

Fig. 2.—The foot of the mother of the entire family, illustrating a typical rigid type of pes cavus with a tendency to the formation of claw-toes.

lower extremities. The Romberg sign is negative and there are no tremors. The feet show a moderate degree of pes cavus. The deformity is fairly rigid and numerous callosities are already developed. He presents normal coordinative functions. The reflex system shows that the Achilles and patellar reflexes are absent. No plantar flexion is obtained when the plantar surface of the feet is scratched, but there is some fanning of the small toes in each foot. There are no disturbances in sensibility and no interference with the deep proprioceptive type of sensation. He presents no nystagmus. The pupils react to light and in accommodation and there is no defect in speech.

CASE 3.—A boy, aged 19, one of twins, the other of which died at the age of 5 months of pneumonia, presents no systemic abnormalities. He has no ataxia or incoordination. No vertebral disturbance is present and no scoliosis can be made out. He presents no swaying in the Romberg position. He has normal muscle power in both upper and lower extremities. A slight cavus deformity is seen in both feet, with moderate rigidity and moderate callosities. The reflex systems show that the Achilles and patellar reflexes are absent, while there is

fanning in the small toes of both feet. There are no sensory disturbances, muscle tendon and vibratory sensibility being normal. He presents no nystagmus, the pupils are equal and regular and react to light and in accommodation, and no speech defect is demonstrated. At the age of 16 a subcutaneous tenotomy of the plantar fascia was performed, and this has prevented the development of a more severe type of cavus than he shows at present.

Case 4.—In a girl, now aged 18, the parents noticed the beginning of a slight deformity in the feet at the age of 10, which progressed to the production of a considerable degree of cavus. Apparently it has not progressed during the last year. Systemic examination is also negative. She develops no ataxia and does not sway in the Romberg position. She presents no disturbance in muscle power; there is no vertebral deformity. The feet present a marked cavus deformity, which is moderately rigid, and a considerable degree of callosity development. The Achilles and patellar reflexes are absent while the fanning sign is present in both feet. There are no disturbances in sensation, and muscle tendon sensibility is normal. She does not present nystagmus or pupillary or articulatory changes.

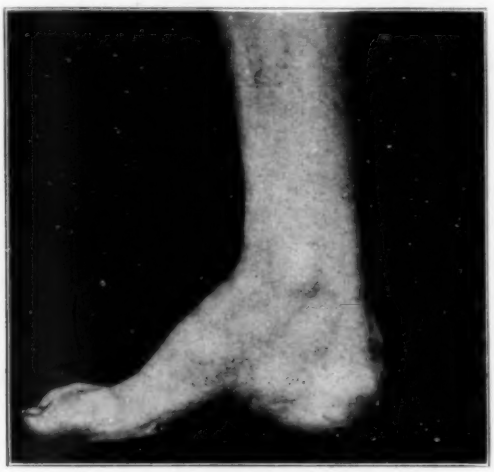

Fig. 3.—The pes cavus modified by the subastragalar arthrodesis.

Case 5.—In a girl, now aged 15, one of a pair of dissimilar twins, the onset of the disease occurred at the age of 10 and rapidly progressed for four years. During the last year there has been no sign of progression. Systemic examination is also negative. She does not present scoliosis and has apparently normal muscle power in both upper and lower extremities. She presents a marked cavus with definite rigidity and the development of callosities. No ataxia and no Romberg sign are present. The Achilles and patellar reflexes are absent and there is fanning in the toes of both feet. Sensation is normal. This patient presents a slight suggestion of a nystagmus, there being some unequal oscillatory movement on lateral gaze to either side. Her pupillary reflexes are normal, and there is no speech defect. She presents a transitory tremor in both hands and feet. In this patient a double subastragalar arthrodesis has resulted in a much improved distribution of the weight on the feet and relieved the patient from the pain of the callosities. Her dissimilar twin sister shows no signs which would indicate the presence of the disease.

CASE 6.—In a boy, now aged 12, the disturbance in the feet appeared at the age of 10, when the cavus was first noticed. This has progressed in severity and continues to increase. The systemic examination is negative. He presents no scoliosis or vertebral deformities. He has no incoordination. He presents a moderate cavus with slight rigidity and no callosities. The muscle tendon sensibility of the upper and lower extremities is apparently normal. The patellar reflex is absent while the Achilles reflex is apparently diminished. The fanning sign is positive. There are no sensory defects. He does not present nystagmus and he has no speech defect. The Romberg sign is not present.

CASE 7.—In a girl, aged 6, belonging to the third affected generation, nothing abnormal has been noticed by the parents. Systemic examination is negative. The child presents a very moderate degree of cavus. The Achilles and patellar reflexes are diminished while the Babinski sign is only very suggestively positive. There is no disturbance in sensation. No nystagmus and no speech defects are found.

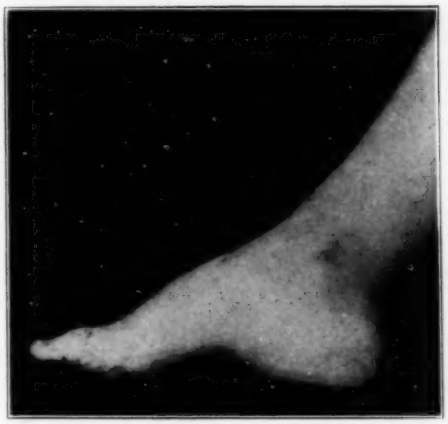

Fig. 4.—The pes cavus in case 6; the cavus is well established, but the foot is not rigid and no claw position of the toes has been established.

CASE 8.—In a girl, aged 4, a sister of the preceding patient, nothing unusual has been noticed by the parents. The systemic examination is negative. No vertebral deformity is present, but there is a slight cavus deformity without rigidity. The Achilles and patellar reflexes are both diminished and a positive fanning sign is present. There is no disturbance in muscle sensibility and the other types of sensation are unimpaired.

COMMENT

In considering this family we find three generations showing a disease which presents many of the characteristics of an hereditary familial disease. This disease begins, as does the typical Friedreich's disease, with some disturbance in gait and the development of the foot deformity, a pes cavus. The process advances sufficiently to destroy the reflex arc controlling the deep tendon reflexes of the knee and ankle, probably through the degeneration of the collaterals which sweep forward from

the entrance of the dorsal roots into the spinal cord to end about the ventral horn cells or intercalated cells thus completing the reflex arc. The process then advances and involves the reflex arc controlling the reaction of the toes to stimulation applied to the plantar surface of the foot, so that the normal plantar flexion is lost and a clear-cut Babinski sign, a fanning reaction or failure of the toes to present the normal plantar flexion results. The degeneration terminates apparently at this point and the other characteristics of the disease, the ataxia, the scoliosis, the nystagmus and the dysarthria, fail to develop.

The degenerative tendency is apparently weakening, for the most definite signs are elicited in the grandmother, the second and third generation showing an anticipation and failing to develop as marked a syndrome.

DISCUSSION

DR. RILEY: I may speak briefly of the literature. In the Surgeon General's catalogue I could find reference to only one article calling attention to the occurrence of such a condition. This appeared in an Italian journal, published in Naples, to which I have not as yet secured access. Oppenheim states that abortive cases are known to occur, but in most textbooks there is no reference to abortive types of Friedreich's ataxia. We have presented this family with what is really a lumbar Friedreich's ataxia, to establish the occurrence of this symptom-complex.

DR. BERNARD SACHS: The point which Dr. Riley raises interests me, and that is whether it is worth while to establish an abortive type of Friedreich's disease. I think there is nothing astonishing in seeing cases of familial disease in which not all the symptoms are fully developed; that is practically what an abortive type of such a disease as this would mean. The characteristic feature about the patients mentioned here is that the disease begins with a pes cavus; that is of great interest as there are very few diseases which begin in that way. Only two other diseases would have to be considered at all. Pes cavus, or something which approaches clubfoot, is characteristic of Friedreich's disease and is also characteristic of the Charcot-Marie-Tooth disease, and there are families in which something like a congenital clubfoot occurs and nothing else. It is rather anomalous for Friedreich's disease to be stationary for a period of thirty years, as I think was the case in the mother presented here. The general symptomatology, I have no doubt, though I have not gone into the matter carefully here, is in line with Friedreich's disease, although nothing was said about the behavior of the pupils.

The point I would like to insist on is that in all familial diseases, especially in those of degenerative type, there may be all sorts of combinations of symptoms and of degenerations. One striking symptom-complex I have seen was an association of what appeared to be progressive muscular atrophy of the hand with symptoms in the lower extremities characteristic of Friedreich's disease.

In Friedreich's disease the psychic defect is striking. In the persons of the two generations we saw here, the psychic defect was not marked, if it was present at all. We must not draw the lines of the clinical picture of an hereditary familial disease too close. Variations from the type are almost

certain to appear. The only question is whether the number of characteristic symptoms is sufficient to warrant this being described as an abortive form of Friedreich's disease. To my mind it represents something beginning like Friedreich's disease in several generations, and it would be important to know that not all the symptoms are present in these cases.

DR. SMITH ELY JELLIFFE: First, I think it is not without interest to call attention to the fact that this year, 1925, is the one hundredth anniversary of Friedreich's birth; Charcot and Friedreich were both born one hundred years ago. Second, it strikes me that the opportunity for judging cases of this kind is fraught with great interest. Dr. Riley knows with what difficulty we brought together the symposium on hereditary and heredofamilial disease for the Association for Research in Nervous and Mental Diseases. He knows with what vigor I assailed him, as secretary, about the title given to my referat, namely, whether these heredofamilial diseases of the nervous system showed dominant or recessive characters. I said we were not in a position to formulate any such problem, for up to the present, from the mendelian point of view, we did not have enough information. Although it might appear on the surface from the charts shown by Dr. Rombold that dominant factors had passed down through three generations, still those charts do not provide enough information concerning the collateral branches to settle the question as to whether dominant or recessive factors have entered into the heredity of this disturbance.

As to the question of types in general, from my point of view there is no such thing as "Friedreich's disease." Practically all classifications are only useful "fictions." They deal with groups of symptoms which Friedreich originally pointed out, and to which he gave a thoroughly artificial, though useful, "classical" picture. Since then the unthinking among us have been trying to identify everything which appeared as he described it and construct a "clinical disease" as a bit of reality. But there is an enormous number of variations, aberrant types, if one so wishes to phrase it, and that must be so, as Dr. Sachs has said, in most of the heredo-degenerations.

In comment on Dr. Riley's statement about the absence of literature on these types, I am a little surprised that he did not run across Hanhart's studies in Switzerland on families with Friedreich's disease. Hanhart collected all known cases of the disease in Switzerland. In certain of the families there is an interesting point bearing on the general lethal factor of incest. That gives the impression that a lethal factor is introduced by some recessive process in the genesis of the complex of functions which we know is closely related to equilibrium. The stimuli come up through the receptor neurons through the spinal cord and are more or less correlated in the cerebellar regions. We find certain groups in which the cerebellar components are more involved than are the spinal components. This Dr. White and I have emphasized (Diseases of the Nervous System, ed. 4, pp. 646 and 654).

DR. JOSHUA ROSETT: Everybody will agree with Dr. Sachs that variations in the particular symptomatology of a given hereditary disease are to be expected. But how are we to account for a variation in the symptomatology of a disease which manifests itself, as in this case, in an affection of the osseous system of the foot in some members of the family, and in a diminution or disappearance of the patellar reflex in others; in a sign of Babinski in some and in typical ataxia in others? Surely not by an inherited malformation of any one system, for as a matter of fact the parent from whom the various manifestations of the disease were inherited exhibited some of them, but not

all. A rational hypothesis appears to me to be the inheritance of a unit factor — some poison — which exists in the body fluids of the members of the affected family, and which strikes one system or another according to the special susceptibility of the individual. In a study of Thomsen's disease some years ago, I found variations of a similarly wide scope. Some members were psychotic without any muscular abnormality. Some had lost the patellar reflex. Some were affected with severe pains in the lower limbs. Others exhibited the manifestations of the muscular abnormality; and the degree of the abnormality and the special mode by which it could be elicited differed in the several individuals within wide limits. In that case, too, a rational mode of accounting for the various manifestations of the inherited disease is by the assumption of a nocuous inherited agency, which is to be found in some of the body fluids, and which affects one system or another according to the grouping of the other inherited units, that is to say, according to particular susceptibility of the person. Such an inherited unit factor may be legitimately called a sublethal factor. A lethal factor has been established by students of heredity in certain forms of the *Chrysophila* fly. From such a standpoint we must look with suspicion on any extraordinary number of deaths in such a family, irrespective of the immediate cause of death. The fact that a number of children in this family died from such a common affection as pneumonia does invalidate the suspicion that the pneumonia proved lethal only in cooperation with the inherited sublethal factor in possession of the members of the stricken family.

Dr. Riley: I have nothing further to say except that, as Dr. Sachs has pointed out, there are complete transitional forms between all related types of disease, but this does not seem to me to fall exactly into the category of a transitional form. Friedreich's ataxia, as a rule, begins in early adolescence and progresses almost inevitably to a fatal termination as the result of some sort of intercurrent disease after the primary condition has existed for a considerable length of time. This syndrome which we have presented tonight is a Friedreich fragment. It appears as does the typical Friedreich's disease, but comes to a spontaneous cessation after the development of a few symptoms and physical signs; on account of this fact and the paucity of published records, it was considered justifiable to present this family.

THEORY OF THE MECHANISM FOR THE BABINSKI TOE PHENOMENON*

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Since Babinski's first description of the big toe phenomenon as a sign of disturbed function of the pyramidal tracts, many theories as to its mechanism have been propounded. In the available literature we were unable to find any of these theories that would be satisfactory—at least to us. In reading Babinski's original papers, one is struck by his failure to offer any explanation for the mechanism of his phenomenon.

In routine neurologic examinations of cases of disease of the central nervous system, great variations are frequently noted in the response of the big toe to plantar stimulation. Among these are: Dorsiflexion of the big toe without stimulation, i. e., spontaneously, which is observed in diseases included in the so-called amyostatic symptom-complex (extrapyramidal system), the so-called chronic Babinski sign; spontaneous, constant, vermicular, slow, rhythmic movement of the big toe in dorsiflexion simulating an athetoid movement—this type of reaction may be designated as "the athetoid toe phenomenon;" it is frequently observed in some of the hyperkinetic syndromes of the extrapyramidal system such as the athetoses, the dystonias, the choreas and some forms of Little's disease; and finally, certain cases of definite involvement of the pyramidal tracts are occasionally encountered in which plantar stimulation evokes neither dorisflexion nor plantar flexion of the big toe.

It is not within the scope of this communication to discuss the technic of obtaining the Babinski phenomenon or its confirmatory signs and their clinical evaluation.

The classic Babinski phenomenon observed in pure lesions of the pyramidal tract consists of dorsiflexion of the big toe with fanning and plantar flexion of the remaining toes on stimulation of the sole of the foot. Stimulation of the sole of the foot evokes a motor response which depends on the integrity of the final common pathway of the motor system—the anterior horn cells of the spinal cord. For the orderly execution of this movement it is essential that the higher centers influencing this common pathway be intact; i. e., that there be anatomic and physiologic cooperation between the corticospinal and extrapyramidal systems.

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The oldest pattern for posture of all the toes is plantar flexion. This is evidenced in animals like the rodents in which the feet are usually provided with five toes, all of which are armed with claws; the hallux does not differ in form from the other digits. Ascending the mammalian scale, we find that the anthropoids and also the half apes, differ from man in having the great toe so constructed as to be able to oppose the other toes (much as our thumb can oppose the fingers), instead of being parallel with the other toes and adapted for supporting the body on the ground. The prehensile character of the hallux is fully maintained even in those animals which, like the baboons, are terrestrial rather than arboreal in their habits and are quite quadrupedal in their mode of progression.

If we accept, with Professor Owen, as the definition of the word "foot," *an extremity in which the big toe forms the fulcrum in standing or walking (in maintaining the erect posture)*, then man alone has a pair of feet. Anatomically, however, the foot of apes and half apes agrees far more with the foot of man than with his hand, and similarly, the ape's hand resembles man's hand and differs from his foot. Physiologically, the hand throughout the whole order of primates remains the special, prehensile organ, whereas the predominant function of the foot, however prehensile it may be, is constantly locomotion. The great toe in apes is never as rudimentary as the thumb; it is never, as it often is in man, the longest digit of the foot, but is constantly the shortest one. Whereas in many of the lower animals, the big toe is capable of isolated extension, flexion, abduction and adduction, in man this toe is capable only of two isolated movements, dorsiflexion and plantar flexion. In harmony with his structure, the orang rarely assumes a truly erect posture; his legs being exceedingly short he walks resting on the knuckles of his hands and the outer borders of his feet. His feet have exceedingly long toes except the hallux which only reaches to the middle of the proximal phalanx of the index digit of the foot. In the course of later development, when the animal is beginning to approximate the erect posture (peculiar to man, who alone has two feet), the big toe is found to have grown and become the fulcrum. It is here that structure follows function in that the big toe loses its comparatively rudimentary character and becomes larger, longer and plantigrade.

According to Keith, there is abundant evidence geologically to justify the presumption that "man and the gorilla are both evolving, but in opposite direction; the one towards brain and the other towards brawn . . . . a strict comparison of the structural characteristics of the feet of man, the gorilla and the chimpanzee, leaves the anatomist convinced that the human foot in the course of its final evolution passes through a gorilline stage . . . . the gorilla's feet have advanced

nearer to human shape than those of any other ape, but the gorilla still walks with a forward slant in his body supporting and balancing his weight on his bent knuckles as he advances." Lamarch (1809), and Darwin (1871) assume that if an anthropoid ape became, either from choice or necessity, a ground living form, it would, in the course of generations, acquire a human gait. If then, the essential characteristics of the human foot are the relatively great size and length of the big toe and the relative shortness of the other four digits, then the gorilla's foot stands intermediate between that of the chimpanzee and that of the human.

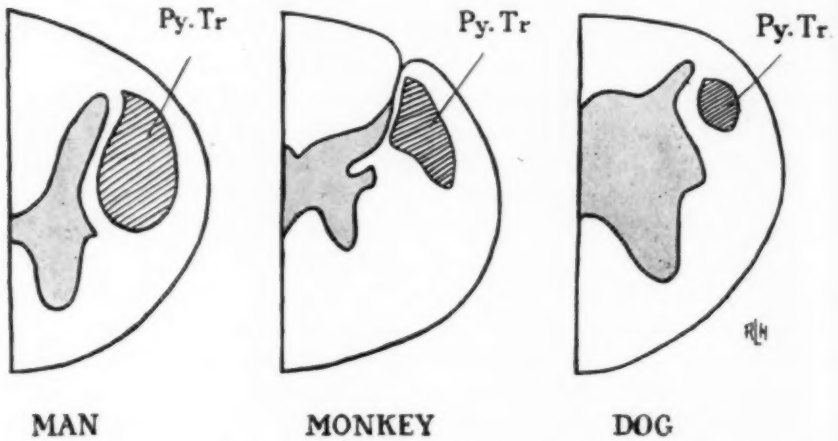
In view of what has thus far been said, we are justified in assuming that dorsiflexion of the big toe and plantar flexion of the smaller toes is the posture of the digits for animals that utilize all four limbs for locomotion. Ascending gradually in the animal scale to that stage at which erect posture becomes an important element of adjustment to the environment, we find that the structure and position of the toes simulate those of man. Simultaneously with this adjustment for erect posture, we also find that there is a close relationship between the size of the corticospinal pathways and such adjustment; that is, in carnivora in which the approach to the erect posture is almost nil, the corticospinal fibers are not as numerous as in primates; in ungulata the fibers of the "pyramid tract" that reach the cord are small in number, and these do not descend farther than the upper cervical segments. Furthermore, King after carefully localizing and extirpating the motor area in one hemisphere of the sheep, traced the resulting degeneration by the Marchi method and found the "pyramid tract" to be comparatively insignificant. This is well illustrated by the accompanying diagram showing the relative size of the pyramidal tract in the dog, monkey and man.

It is well established that the corticospinal system has developed at the expense of the extrapyramidal system, so that with the evolution and progressive increase in the development of the cerebral hemispheres, some of the function of the extrapyramidal system, especially the striatum, is delegated to the pyramidal system, or as Tilney and Riley say "the striatum has become subordinate in action to the dominant neopallium."

Since dorsiflexion of the big toe is the posture in animals whose extrapyramidal system is the predominant efferent pathway, and since with the development of the pyramidal system, the foot became plantigrade with the big toe as a fulcrum for the erect posture, we may further assume that these two pathways are the influences in maintaining, among other things, the posture for the big toe in man. Normally, with the fine balancing of these two systems, the big toe is neither in flexion nor in extension, so that with the falling out of pyramidal

influences the extrapyramidal influences come into play, with a reversion to the old posture; i. e., dorsiflexion of the big toe. In other words, although dorsiflexion of the big toe is indicative of disturbance of pyramidal influences, it is also evidence of a preponderance of extrapyramidal influences. On stimulating the sole of the foot, however, we find, normally, plantar flexion of the big toe; this is due to a preponderance of the influences of the more recently developed pyramidal system.

This theory of the mechanism of the Babinski phenomenon finds substantiation in a number of well established clinical facts. In newborn infants dorsiflexion of the big toe occurs normally on stimulation of the sole of the foot. Here, with the incomplete myelinization of the



Relative size of the pyramidal tract in the man, monkey and dog; level of the fifth thoracic segment of the spinal cord (after Sherrington); *Py. Tr.*, pyramidal tract.

pyramidal tracts, and the infant's inability to maintain completely the erect posture, this toe reaction simply represents a reversion to "early" posture, due, we believe, to a preponderating influence of the extrapyramidal system.

Dorsiflexion of the big toe in pure pyramidal tract lesions giving rise to hemiplegia depends on the preponderance of extrapyramidal over pyramidal influences; i. e., with the falling out of the latter, the former, unopposed in their effect, come into play.

The occurrence of a continuous, spontaneous dorsiflexion of the big toe, the so-called chronic Babinski sign, in pure extrapyramidal diseases would seem to offer additional evidence in substantiation of our theory, because, here, the pyramidal tracts being intact, there is over-activity of the extrapyramidal system. Furthermore, stimulation of the sole

of the foot in these cases gives rise to plantar flexion, bringing back into play the influences of the intact pyramidal tract. It is needless to say that this applies only to irritative lesions of the extrapyramidal system; destructive lesions of the extrapyramidal system do not give rise to a chronic Babinski sign, and on stimulation of the sole of the foot the response is plantar flexion.

Closely allied to the chronic Babinski phenomenon, which is phasic, is what we have referred to in the early part of the paper as the "athetoid toe phenomenon;" this is merely a kinetic manifestation of the chronic Babinski sign, the actual mechanism in operation being practically the same for both.

In cases with slight involvement of the pyramidal tracts, plantar stimulation is followed by neither dorsiflexion nor plantar flexion of the big toe. Here the usual preponderance of the pyramidal over the extrapyramidal influences being reduced, an actual balancing between the two occurs so that the toe remains in normal posture. The finding of such a response (actually neither plantar nor dorsal flexion) is just as pathologic as dorsiflexion.

Finally, it is needless to say that the same mechanism is applicable in explanation of the big toe phenomenon in lesions of the pyramidal tracts in the spinal cord. In complete transverse lesions of the cord, however, the appearance of dorsiflexion of the big toe in plantar stimulation has been observed at times. Since the presence of postural reflexes in such lesions depends on their extent and severity, when dorsiflexion of the big toe does occur, it may be assumed to indicate an incomplete division of the cord, with retention of the older extrapyramidal at the expense of the more recent, and consequently more vulnerable, pyramidal influences.

CONCLUSIONS

1. The Babinski toe phenomenon represents a posture of the toes, particularly the big toe, depending on: the integrity of the final common motor pathway, the intactness of the sensory component of the reflex arc for the motor response and the influences exerted on the latter by the pyramidal and extrapyramidal systems.

2. Normally, the posture of the toes in man is plantar flexion.

3. Dorsiflexion of the big toe represents a reversion to normal posture of the foot in all primates excepting man.

4. Ascending the mammalian scale, it is found that the acquisition of the big toe is simultaneous with a functional adjustment necessary for the change from an aquatic and arboreal to a terrestrial existence.

5. The maintenance of erect posture goes hand in hand with this adjustment and requires a plantigrade foot with the big toe as the fulcrum.

6. This adjustment must necessarily be associated with a neural apparatus as its basis and consists of the influences of the pyramidal and extrapyramidal systems in a state of a well balanced equilibrium.

7. This is borne out anatomically by a graded preponderance of the pyramidal over extrapyramidal systems as the animal scale is ascended, finding a higher expression in the primates in general and the highest in man.

8. Removal of the pyramidal influences gives rise to a reversion to a lower scale with a preponderating influence of the extrapyramidal system. This reversion finds expression in the original dorsiflexion of the big toe; i. e., the Babinski toe phenomenon.

INTRACRANIAL PRESSURE CHANGES DURING FORCED DRAINAGE OF THE CENTRAL NERVOUS SYSTEM *

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In recent studies of the cellular response of the central nervous system to subarachnoid injections of trypan blue, four facts developed which gave rise to this investigation (Kubie and Shults [1]): (*a*) Early in the acute stage of a meningeal irritation, and throughout all later stages, the perivascular spaces and many minute crevices of the central nervous system become lined with small mononuclear cells which we believe to be lymphocytes. (*b*) Prolonged drainage of the subarachnoid space during the meningeal reaction is accompanied by a gradual alteration of the proportions of the various cells of the cerebrospinal fluid; the lymphocytes increase in relative abundance in the late fractions of the fluid, and finally, in many cases, far outnumber the other elements. (*c*) Intravenous injections of isotonic or hypotonic solutions which are begun when the spontaneous flow of fluid has almost ceased are accompanied by a renewed outflow of fluid, and a still greater increase in the percentage of lymphocytes. (*d*) Sections from the central nervous system of animals treated in this way show that the perivascular plugs of lymphocytes are largely extruded into the subarachnoid space, and must be the source of the increasing proportion of these cells.

As far as we are aware, these changes have not been previously noted. Differences in the total cell count in several fractions of spinal fluid in man have been reported by various observers (among them Weigeldt, Eskuchen [2] and Cestan, Gay and Peres [3]). Despite the fact that similar differences occur in quadrupeds, these variations are always explained as a result of sedimentation. It is interesting that the last mentioned observers made a few differential counts of the cells in the counting-chamber, as well as total counts. Without their recognizing

* From the Department of Physiology of the Johns Hopkins Medical School.

1. Kubie, L. S., and Shults, G. M.: Vital and Supravital Studies of the Cells of the Cerebrospinal Fluid and of the Meninges in Cats, Bull. Johns Hopkins Hosp. **37**:91 (Aug.) 1925.

2. Eskuchen, K.: "Ist die fraktionierte Liquoruntersuchung prinzipiell zu fordern?" München. med. Wchnschr. **69**:1536 (Nov. 3) 1922.

3. Cestan, R.; Gay, M., and Peres, M.: Quelques considerations sur la valeur décroissante de la cytose du liquide céphalo-rachidien retiré par la ponction lombaire, Encéphale **19**:409 (July-Aug.) 1924.

the significance of the observation, three out of the four counts of this kind which they made on patients with sterile meningitis showed an increase in the lymphocytes in the late fractions, while the other elements and the total counts decreased. Furthermore, Dr. Perrin H. Long in the Boston City Hospital has followed up the experimental studies of Kubie and Shults [1] with an analysis of the cerebrospinal fluid of patients, using the same supravital technic. In a surprisingly wide variety of pathologic conditions he too has found that the lymphocytes become increasingly preponderant in the late fractions of the fluid.

These findings suggested the possibility that this elimination of cellular exudates might have some influence, perhaps beneficial, on the course of certain central nervous system infections. It was clear, however, that one would hesitate to produce any marked increase in intracranial pressure in the presence of central nervous system disease. With this in mind, the present studies were undertaken in order to determine: (*a*) whether injections of hypotonic or isotonic solutions cause a serious increase in intracranial pressure when the cerebrospinal fluid is allowed to escape freely, and (*b*) whether fluids administered in any other way than by intravenous injection can have a similar action.

I. EXPERIMENTAL PROCEDURE

In these experiments, it was necessary to follow the changes in intracranial pressure while allowing the cerebrospinal fluid to escape freely from the cisterna. A method had to be used, therefore, which was anatomically independent of the cerebrospinal fluid itself. It is necessary to present the procedure in detail, because it was only by attention to these details, and after repeated failures, that unequivocal results were secured. All experiments were performed on dogs.

1. Sodium barbital, 0.3 Gm. per kilogram, was injected intravenously, about one hour before operating.

2. With blunt dissection, the occipito-atlantoid ligament was exposed, spreading the heavy muscles of the neck with a small powerful retractor. (In the earlier experiments, cisternal puncture through the skin was performed in the usual way; but in experiments of so many hours' duration it frequently happened that a sudden twitch of the deep muscles would dislocate the needle. Repuncturing under such circumstances is difficult, because there may be little fluid left in the cisterna to indicate when one has reentered, and because one is likely to make a second hole in the ligament and dura, in which event all further observations on pressure or on the flow of fluid become of no value. With the occipito-atlantoid ligament exposed, however, the constant presence of the needle in the cisterna is assured; and in all of the final experiments on which our conclusions are based this method was used.)

3. The midline incision in the neck was now continued forward over the cranium to the root of the nose, and the animal was placed on his right side. The left temporal muscle was freed from its medial and posterior attachments and reflected laterally. A hole was then trephined in the left parietal bone, avoiding all the larger venous channels in the bone by keeping at least 0.5 cm. in front of the parieto-occipital suture, and at least 1.5 cm. lateral from the midline. It was absolutely essential that all bleeding from the under surface of the bone should be checked before the dura was opened. This was accomplished with bone-wax, hot saline and bits of muscle. If this was not done carefully, bleeding would recommence under the influence of the injection, invalidating all further pressure readings.

4. Before opening the dura under the trephine hole, the cisterna was punctured through the exposed occipito-atlantoid ligament with a 16-gage lumbar puncture needle. A manometer, of 1.0 mm. bore, was immediately joined to the needle by a metal, three-way adaptor. (This made it possible either to register cisternal pressure or to drain the canal by a mere turn of the stop-cock.) Thus, in each experiment the first observation made was the cerebrospinal fluid pressure in the cisterna.

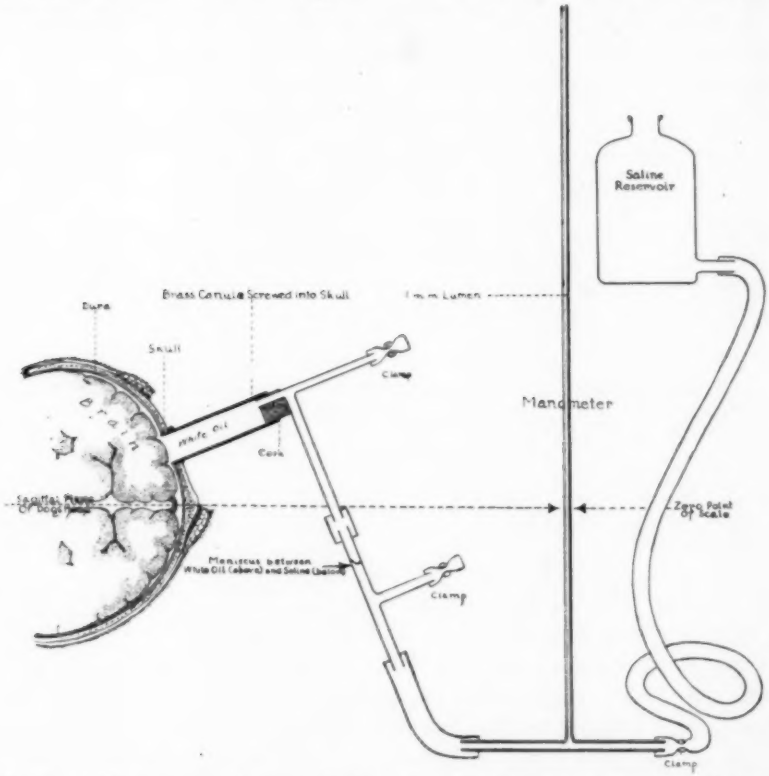
Preliminary tests were made on several animals in which the pressure in the cisterna was observed before, during and after trephining the skull. These showed that, except in certain rare instances in which for some reason the initial pressure in the cisterna was over 200 mm., opening the skull caused no change in the cisternal pressure. This pressure was taken, therefore, as the true intracranial pressure.

5. By this time the field under the trephine hole would have become thoroughly dry, so that the dura could be incised. The opening of the dura was done with the greatest care to avoid injury to the underlying pia-arachnoid. A fine hook was caught in the fibers of the outer dural surface, and by means of this the membrane was lifted well away from the surface of the brain. A hole was then scratched gently through it with the edge of a knife. As the dura thinned out, but before it had actually opened, fluid would begin to ooze through the meshes; when it was finally opened, a small amount of fluid poured out into the wound. Because this fluid oozed through the still unopened dura, when the arachnoid could not possibly have been punctured—and because of the evidence recently brought by Penfield [4]—we felt that it was clearly subdural and not true subarachnoid fluid. During the further excision of the dura the underlying structures were protected

4. Penfield, W. G.: The Cranial Subdural Space, Anat. Rec. **28**:173 (July) 1924.

with a blunt, flat instrument, so that we are confident that the cannula opened into the subdural but not into the subarachnoid space.

Into the trephine hole a specially constructed brass cannula was then screwed. The thread of this cannula tapered, so that the ends would just engage with the opening made by the trephine used. To further seal the joint, the threads were thickly coated with Fleck's "perfected" red dental cement just before the cannula was screwed into place. This cement dried within a few minutes, making an absolutely tight joint. The cannula was 4.5 cm. long, and had a lumen 1.5 cm. in diameter.



Intracranial pressure changes during forced drainage of the central nervous system.

After the cement dried, the cannula was filled with warm white-oil. This was used instead of saline to eliminate any osmotic interchange between the subarachnoid fluid and the fluid in the manometer system. The white oil was led through the series of connections illustrated in the diagram to a vertical glass tube, where it rested on the column of salt solution that led to the 1.0 mm. bore manometer. Despite the inertia of such a system, the manometer registered pressure oscillations of from 2 to 5 mm. with each heart beat, and from 10 to 40 mm. with each respiration.

The zero points of both manometer scales were adjusted to the sagittal plane of the animal.

6. When the dura was opened, the pressure in the cisterna would usually drop a few millimeters; but when the cranial manometer was brought to the pressure found originally in the cisterna, this initial pressure would be restored. (This may not give absolutely exact levels for the intracranial pressure; but after experimenting with various other approaches this was found to be the most satisfactory that we could devise, and certainly approaches true values closely.)

7. The sensitivity of the cranial manometer, and the freedom of its responses to known pressure changes were then tested by the alternate raising and lowering of the pressure in the cisterna. The responses were tested through a range of pressures far greater than that encountered in any of the experiments; and in any case in which the cranial manometer failed to follow the cisternal pressure closely and with reasonable promptness, the experiment was discarded. Such failures occurred only at the outset, however, and could always be traced to a leak, to air trapped in the system or to the formation of a blood clot in the lumen of the cannula.

8. If the effect of an intravenous injection on intracranial pressure was to be tested with no fluid escaping from the cerebrospinal spaces, a base-line of normal pressure was now established by following the intracranial and the cisternal pressures for about one hour and recording pressures every five minutes, after which the injection was given and pressure changes were recorded every minute throughout the injection, and again every five minutes during the succeeding hour or two.

If, on the other hand, the aim of the experiment was to determine the pressure changes with the fluid escaping freely, a preliminary period of observation of about fifteen minutes was allowed, and then the cisterna was drained. When the cisterna was drained, the pressure in the cranial manometer fell sharply to such an extent that at the end of each inspiration the manometer would register anywhere from 0 to 50 mm., and at the end of expiration anywhere from 20 to 70 mm. Each animal, however, would arrive at some quite constant level which was recorded for from one half to three quarters of an hour before the injection was given.

9. Again at the end of the experiment the test for the sensitivity of the cranial manometer was repeated and finally, the cranium was opened widely and examined for evidences of bleeding. This was to insure that the manometer had been free to register fully any pressure changes that had occurred during the experiment, and to rule out extravasated blood as a source for any increase in pressure which had occurred.

10. The injections used were distilled water, 0.47 per cent saline solution (which, while hypotonic to the blood, is just above the hemolysis point of dog's red blood cells) and 0.9 per cent saline solution. Injections of Ringer's solution, and of urea and sugar solutions, have also been used for various purposes, but give no added information and are not included in the data of this report. For making the injections, the duNöuy pump and the hot-cabinet were used, as described in the recent studies on the chemistry of the fluid (Kubie and Shults [5]). This enabled us to control very accurately the rate as well as the volume of injection, and the temperature of the injection fluid.

II. RESULTS

1. So many variables enter into the reactions of animals to intravenous injections, that it is not surprising to find that the change in intracranial pressure bears no constant relationship to the volume or rate of injection of any one solution. This is illustrated in the experiments from which the essential points are presented in table 1.

TABLE 1.—*The Lack of Correlation Between the Rate or Volume of Injection and the Magnitude of the Resulting Pressure Change*

Weight in Kg.	Volume of 0.9% Saline Solution Injected, Cc. per Kg.	Rate in Cc. per Kilogram per Minute	Intracranial Pressures in Millimeters of 0.9% Saline Solution*		
			Before Injection	At End of Injection	15 Minutes After
13.6	62.5	4.8	65	142	132
17.3	40.5	3.7	70	160	140
16.2	30.9	5.2	20	33	30
16.4	30.5	5.1	70	140	115
13.0	34.6	6.9	62	102	92

* In this and the subsequent table the pressures given are the maximum pressures at the end of the expiratory pause. This exaggerates the pressures, but at the same time gives a more constant and comparable group of records, as the inspiratory drop, in the same animal during a single experiment, and almost from minute to minute, sometimes varied from 10 to 60 or 70 mm.

A comparison of the injections made into the first two animals illustrates the fact that a smaller, slower injection can give a larger pressure increase. The second group shows closely similar injections giving an exceedingly wide range of response.

Furthermore, in all five of these experiments, the fluid was draining from the cisterna throughout the injection; and the volume of cerebrospinal fluid expelled from the canal bore no relationship either to the volume or rate of injection or to the degree of pressure alteration. But the outflow of fluid from the canal is dependent on so many accidental variants other than its rate of formation and absorption that this result is even less surprising.

5. Kubie, L. S., and Shults, G. M.: Studies on the Relationship of the Chemical Constituents of Blood and Cerebrospinal Fluid, J. Exper. Med. **42**:565 (Oct.) 1925.

2. The rise of intracranial pressure which occurs when solutions which are isotonic or hypotonic to the blood are injected intravenously (Weed and McKibben,[6] Weed and Hughson [7]) takes place even when the cerebrospinal fluid is allowed to drain freely to the outside throughout the experiment. Under these conditions, however, the rise in pressure is usually small; the duration of the pressure plateau is relatively short; and since the initial pressure is reduced by the preliminary drainage to a low point, the maximum pressure attained has in no case exceeded and has only rarely reached the normal range of intracranial pressure of dogs. With the fluid draining, the maximum pressure increase caused by injections of 0.9 per cent saline solution was 90 mm., and the minimum was 13 mm. Under similar conditions, but with an injection of 0.47 per cent saline solution, the maximum change observed was 75 mm. (in an animal which had received two previous injections), and the minimum change observed was 44 mm. In general, the initial pressure change from an injection of 0.9 per cent saline solution is quite as great as that from an injection of 0.47 per cent saline solution (and some times greater), but the return to a low level takes place much more rapidly in the first case than in the second. It is also evident that the hypotonic saline solution, at a concentration which is just sufficient to prevent hemolysis of dog's blood, usually causes far less extreme changes in intracranial pressure than those reported for slower injections of much smaller volumes of distilled water (Weed, et al.).

The three experiments presented in table 2, are typical experiments. They illustrate the general range of pressures which we have encountered. It will be observed that in the experiments in which 0.47 per cent and 0.9 per cent saline solution were injected, the initial pressure just before the injection, with the cisterna closed, is quite low. This lowering of the cisternal pressure was deliberately produced in these two experiments by a preliminary partial drainage of the canal, in order to have the two responses (i. e., first with the cisterna closed and later with it draining) start at nearly the same point. The table illustrates well the essential similarity of the response to 0.47 per cent and 0.9 per cent saline solution, and the disproportionately greater response to an

6. Weed, L. H., and McKibben, P. S.: Experimental Alteration of Brain Bulk, Am. J. Physiol. **48**:531 (May) 1919; Pressure Changes in the Cerebrospinal Fluid Following Intravenous Injection of Solutions of Various Concentrations, ibid. **48**:512 (May) 1919.

7. Weed, L. H., and Hughson, W.: Intracranial Venous Pressure and Cerebrospinal Fluid Pressure as Affected by the Intravenous Injection of Solutions of Various Concentrations, Am. J. Physiol. **58**:101 (Nov.) 1921; Systemic Effects of Intravenous Injection of Solutions of Various Concentrations with Especial Reference to the Cerebrospinal Fluid, ibid **58**:53 (Nov.) 1921.

injection of only half as much distilled water at a slower rate. How much of this difference may be due to the laking of red cells we are not at present in a position to say.

From these and similar experiments, we feel that it is safe to conclude that the increase in intracranial pressure which accompanies intravenous injections of isotonic or hypotonic solutions is of inconsiderable magnitude when the cerebrospinal fluid is allowed to escape during the course of the experiment. And furthermore, that the procedure is quite innocuous, at least to normal animals, is shown by the fact that many dogs were subjected to this treatment repeatedly at intervals of only a few weeks without any injurious effect.

TABLE 2.—*The Effects of Identical Injections on an Animal with the Cisterna Closed and with the Cisterna Draining*

Date,	Weight in Kg.	Experimental Condition	Injection	Volume Cc. per Kg.	Rate in Cc. per Kg. per Min.	Intracranial Pressure in Millimeters of 0.9% Saline Solution						
						Before Injection	At End of Injection	After 15 Min.	After 30 Min.	After 60 Min.	After 90 Min.	After 120 Min.
I												
3/12/26	19.4	Cisterna closed	Distilled water	15.4	2.6	145	190	200	190	180	175	Drained to 65 mm.
3/12/26	19.4	Cisterna draining	Distilled water	15.4	2.6	85	95	100	104	100	90	
II												
3/25/26	15.8	Cisterna closed	0.47% saline solution	31.6	4.0	60	135	135	133	118	118	Drained to 48 mm.
3/25/26	15.8	Cisterna draining	0.47% saline solution	31.6	4.0	46	83	113 (struggling)	112	110	90	70
III												
3/23/26	13.0	Cisterna closed	0.9% saline solution	34.6	6.9	70	144	132	130	120	105	Drained to 45 mm.
3/23/25	13.0	Cisterna draining	0.9% saline solution	34.6	6.9	62	102	92	85	80	70	

III. THE EFFECTS OF FLUIDS BY MOUTH

We are not yet prepared to say exactly how the effects of fluids administered by mouth compare with the effects of intravenous injections. The problem is still under investigation. But from the work already done we can say that tap water gives a definite stimulation, and normal saline solution a response of which we are less certain.

The response to tap water seems to reach its maximum during the latent period before the kidney response begins, and declines as diuresis sets in. This tendency for the intracranial response to reach its height during the period of renal lag and to diminish as diuresis comes on is well illustrated in many of the charts from the papers of Weed and Hughson.[7] But interpretation of the physiologic significance of this must take into account the uncertain effects of anesthesia on kidney function.

An example of this response to tap water by mouth is given in table 3.

TABLE 3.—*The Urinary and Cerebrospinal Fluid Response to Tap-Water Administered by Mouth*

April 1, 1926: Male dog; weight, 13 Kg.; sodium barbital, 0.25 Gm. per Kg., 3/31/26 at 4 p. m.; sodium barbital, 0.06 Gm. per Kg., 4/1/26 at 9 a. m.;* 9:30, bladder catheterized and emptied by aspiration; 10, cisterna punctured.

Time	Manipulation	Cerebrospinal Fluid in Cc.	Urine in Cc.
11:00 to 11:15	.....	1.2	2.0
11:15 to 11:30	.....	0.9	0.0
11:30 to 11:45	.....	0.7	2.5
11:46 to 12:01	Warm tap-water by stomach tube 1,000 cc. administered	1.1	0.0
12:01 to 12:15	.....	1.3	0.8
12:15 to 12:30	.....	2.3	0.8
12:30 to 12:45	.....	2.1	7.0
12:45 to 1:00	.....	0.9	6.5
1:00 to 1:15	.....	1.6	8.0
1:15 to 1:30	.....	0.4	10.0
1:30 to 1:45	.....	0.8	15.0
1:45 to 2:00	.....	0.1	15.0

* This splitting of the anesthesia was done deliberately in order to minimize the renal depression.

COMMENT AND CONCLUSION

Such pressure changes within the head as these represent an algebraic summation of at least three possible variables: the volume of fluid free in the ventricular and subarachnoid spaces, the volume of blood within the whole craniovertebral cavity, and hypothetic changes in the actual bulk of the parenchymatous tissue due to hydration or dehydration of the cells themselves.

There is no way of measuring the last element; but the histologic studies of Weed and McKibben [8] suggest that hydration is a detectable result of intravenous administration of distilled water only when the cranial cavity is kept intact throughout the injection. Therefore, allowing the cerebrospinal fluid to escape, as we have done, diminishes both the hydration factor and the increase in free fluid to a great extent; but the possibility that some fluid may become trapped in the system cannot be ruled out by the methods used.

The attempts to determine the changes in the volume of intracranial blood by determining the changes in intracranial venous and arterial pressures are only partially successful, because the volume of intracranial blood and the pressure under which it is held need by no means change proportionately, nor even in the same direction. These efforts to correlate intracranial and vascular pressures seem frequently to rest on the fallacious assumption that blood pressure means a pressure of the blood on the surrounding tissues, whereas it actually results solely from the tension of the vessel wall on the blood within; so that the correlation is between intracranial blood volume and intracranial pressure, not between the two pressures themselves.

8. Weed and McKibben (footnote 6, second reference pp. 541 and 545).

For the present, therefore, we are content to demonstrate that these combined volume changes give a rise in pressure that in its magnitude is harmless to normal dogs, during intravenous injections, provided the cerebrospinal fluid is allowed to drain freely from the cisterna throughout the experiment.

The possible influence of the procedure on the course of certain types of central nervous system infections will be made the subject of further investigations.

THE SIGNIFICANCE OF GAIN IN WEIGHT IN THE MALARIA TREATMENT OF GENERAL PARALYSIS*

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In a preliminary report, published a year ago, on the malaria treatment of general paralysis,[1] it was mentioned that a large proportion of patients gained considerable weight after completing the course of malaria, and that, on the whole, the patients who did especially well in a clinical sense made a somewhat greater eventual gain in weight than the others. Continued observation of these and of additional patients now makes it possible to say something more definite of the further course of the weight curve in these patients, and to deal less tentatively with the question whether this gain in weight, striking as it often is, has any actual importance in prognosis.

The material on which the present observations are based comprises sixty-two patients whose weight has been recorded at weekly intervals for an extended period of time subsequent to the final malarial paroxysm. Of these sixty-two cases, forty-seven have been followed for six months, thirty-seven for nine months, thirty-three for one year, and eighteen for one and one-half years. In only fifteen cases has this period of observation been less than six months; no case here included has been followed for a shorter interval than three months. In all these patients a diagnosis of general paralysis may be accepted with reasonable certainty.

The base-line from which all gains and losses in weight have been calculated is the final weight of the patient prior to the actual onset of malaria, and this has almost invariably antedated the initial rise of temperature by a few days only. If subsequent gains in weight were calculated on the basis of the patient's initial weight as recorded on the termination of the course of malaria (postdating the final paroxysm usually by some five days), it is evident that an additional factor of variable character would be introduced. Almost every patient in our series—there have been but five exceptions among the total sixty-two—has lost weight during the period of malarial infection; moreover, this loss has been extremely variable, ranging from 3 pounds (1.4 Kg.) or less in eight cases out of fifty-nine to as much as from 12 to 17 pounds (5.5 to 7.7 Kg.) in twelve cases. Furthermore, a time element intro-

* From the New York State Psychiatric Institute, Ward's Island, N. Y.

1. Bunker, H. A., Jr., and Kirby, G. H.: Treatment of General Paralysis by Inoculation with Malaria: A First Report, J. A. M. A. **84**:563 (Feb. 21) 1925.

duces an additional source of confusion; for it has become apparent that whereas some patients begin to regain their lost weight almost immediately after the malarial infection has been terminated, others do not for at least three or four weeks subsequent to the final malarial paroxysm, while still others (numbering about one quarter of this series) continue to lose weight appreciably for more than a week after the malaria has been interrupted. Whereas with but one exception no patient has failed sooner or later to regain at least part of the weight lost during the course of malaria, it is clear that the amount of the handicap under which the subsequent rise in weight began has been too variable in amount and too diversely conditioned to make just allowance for this factor either possible or desirable. As a result of the almost uniform occurrence of this initial weight loss, together with its variability in magnitude and in other respects, thirty of the sixty-two patients in this series were found to weigh less at the end of four weeks from the final malarial paroxysm than they did just before treatment was begun; two patients, however, exactly made up the deficit in this space of time, and thirty weighed more at the end of this interval than they did immediately prior to treatment (table 1, *A*).

TABLE 1.—*Proportion of Patients Above or Below Their Pretreatment Weight at Various Intervals Subsequent to Treatment*

	Above		Below		Unchanged		Total
	No. of Patients	Per-centage	No. of Patients	Per-centage	No. of Patients	Per-centage	No. of Patients
A. Total Group:							
4 weeks	30	48.5	30	48.5	2	3.5	62
8 weeks	45	72.5	17	27.5	0	...	62
3 months	50	81	11	17.5	1	1.5	62
6 months	38	81	9	19	0	...	47
9 months	27	73	9	24.5	1	2.5	37
1 year	23	69.5	9	27	1	3.5	33
1½ years	13	72	5	28	0	...	18
B. Group of 33 Patients Followed Throughout One Year:							
4 weeks	12	36	20	60.5	1	3.5	33
8 weeks	23	70	10	30	0	...	33
3 months	26	79	7	21	0	...	33
6 months	26	79	7	21	0	...	33
9 months	24	72.5	8	24	1	3.5	33
1 year	23	69.5	9	27	1	3.5	33

That gain in weight continued more rapidly from this point onward is indicated by the fact that at the end of eight weeks the number of patients who had failed to reestablish their pretreatment weight had fallen from thirty to seventeen, and forty-five of the sixty-two weighed more at the end of eight weeks than they had when treatment was commenced. At the end of thirteen weeks, the number of patients who had failed to regain their "original" weight numbered only eleven; one patient had exactly equalled his pretreatment weight; and fifty of the sixty-two had surpassed it. At this point—three months subsequent to the termination of the malarial infection—we reach the peak value with

respect to the proportion of patients who registered an advance over their weight as it stood at the beginning of treatment; and this maximum proportion was still maintained at the end of six months.[2]

The first fact, then, which emerges from these observations is that during a period of three months dating from the conclusion of malaria treatment a group of sixty-two patients gained weight to an extent such

TABLE 2.—*Proportion of Patients Above or Below Their Pretreatment Weight at Various Intervals in Relation to Mental Outcome*

	Exceeded Pretreatment Weight		Did Not Exceed Pretreatment Weight	
	No. of Patients	Per-centage	No. of Patients	Per-centage
At 4 Weeks:				
Good remissions (22)	13	59	9	41
Moderate remissions and slightly improved (20)	11	55	7*	35
Total improved (42)	24	57	16	38
Unimproved (20)	6	30	14	70
At 8 Weeks:				
Good remissions (22)	19	86	3	14
Moderate remissions and slightly improved (20)	17	85	3	15
Total improved (42)	36	85.5	6	14.5
Unimproved (20)	9	45	11	55
At 3 Months:				
Good remissions (22)	21	95	1	5
Moderate remissions and slightly improved (20)	19	95	1	5
Total improved (42)	40	95	2	5
Unimproved (20)	10	50	9†	45
At 6 Months:				
Good remissions (17)	15	88	2	12
Moderate remissions and slightly improved (16)	16	100	0	0
Total improved (33)	31	94	2	6
Unimproved (14)	8	57	6	43
At 9 Months:				
Good remissions (15)	12	80	2†	13.5
Moderate remissions and slightly improved (10)	10	100	0	0
Total improved (25)	22	88	2	8
Unimproved (12)	5	41.5	7	58.5
At 1 Year:				
Good remissions (16)	13	81	3	19
Moderate remissions and slightly improved (7)	7	100	0	0
Total improved (23)	20	87	3	13
Unimproved (10)	3	30	6†	60

* Two patients exactly equalled their pretreatment weight.
† One patient exactly equalled his pretreatment weight.

2. Regarding the partial decline in this proportion which then took place (table 1, *A*), it is well to point out that this is not due to the fact that not all the sixty-two patients observed over a period of three months were represented at the later intervals of nine months and one year; for these periods only thirty-seven and thirty-three cases are recorded. Table 1, *B*, which deals solely with the thirty-three patients followed for at least one year, indicates that this latter group exhibits a curve practically identical with the curve for the group as a whole. This moderate decline subsequent to the six months' maximum proportion —from 81 per cent (table 1, *A*), or 79 per cent (table 1, *B*), to 69.5 per cent—is due in large measure to the influence of the "unimproved" cases (table 2); for, whereas 57 per cent of these were above their pretreatment weight at six months, this was true of only 30 per cent at the end of one year.

that the great majority weighed more than they did at the commencement of treatment—and this irrespective of whether simultaneous mental improvement took place during the interval. As will be noted from table 1, *A*, this majority is 81 per cent of the total group; and an identical proportion is found at the end of six months among the forty-seven patients who were followed throughout that time.

Table 2 sets forth the situation from the standpoint of the mental status of the patients; and it immediately appears that among those who underwent no definite improvement in mental condition a much

TABLE 3.—*Average Gain or Loss in Pounds Per Patient As Compared with the Pretreatment Weight at Various Intervals Subsequent to Treatment*

	Good Remissions		Moderate Remissions and Slightly Improved		Total Improved		Unimproved		Worse or Dead		Total Group	
	Gain or Loss	Cases	Gain or Loss	Cases	Gain or Loss	Cases	Gain or Loss	Cases	Gain or Loss	Cases	Gain or Loss	Cases
At 4 weeks.....	1.4	22	2.3	20	1.8	42	—4.1	15	—8.4	5	—0.5	62
At 8 weeks.....	10	22	8.5	20	9.3	42	0.2	15	—5.8	5	5.9	62
At 3 months.....	16.4	22	13.7	20	15.1	42	2.5	15	—9.6	5	10.2	62
At 6 months.....	17.5	17	19.5	16	18.5	33	6.9	11	—18.2	3	13.4	47
At 9 months.....	16.3	15	20.5	10	17.9	25	1.5	10	—37	2	10.5	37
At 1 year.....	15.9	16	22.5	7	17.8	23	—0.2	8	—35	2	10.3	33
At 1½ years.....	10.2	12	17	2	11.2	..	3.4	4	....	..	9.4	18

TABLE 4.—*Percentage of Gain or Loss in Pretreatment Weight at Various Intervals*

	Good Remissions		Moderate Remissions and Slightly Improved		Total Improved		Unimproved		Worse or Dead		Total Group	
	Gain or Loss, %	Cases	Gain or Loss, %	Cases	Gain or Loss, %	Cases	Gain or Loss, %	Cases	Gain or Loss, %	Cases	Gain or Loss, %	Cases
At 4 weeks.....	1.0	22	1.8	20	1.4	42	—2.4	15	—4.8	5	0.0	62
At 8 weeks.....	7.7	22	6.4	20	7.1	42	0.9	15	—2.8	5	4.8	62
At 3 months.....	12.0	22	10.1	20	11.1	42	2.7	15	—5.0	5	7.8	62
At 6 months.....	13.1	17	14.2	16	13.7	33	5.3	11	—9.7	3	10.3	47
At 9 months.....	12.3	15	15.1	10	13.4	25	1.2	10	—18.9	2	8.2	37
At 1 year.....	11.8	16	16.2	7	13.2	23	—0.3	8	—18.4	2	8.0	33
At 1½ years.....	8.0	12	11.1	2	8.5	14	2.0	4	....	..	7.0	18

smaller proportion—about one-half—surpassed their pretreatment weight by the time three months, and also six months, had elapsed. When a separation is made of the patients with complete remissions from those whose mental improvement, though definitely present, was much more moderate in degree, the latter class is in no way to be distinguished from the former with reference to the proportion who at the three-months' and six-months' periods registered an advance over their pretreatment weight. In other words, the percentages which hold throughout the various time intervals for all the mentally improved cases—irrespective of the amount of improvement—are exactly the same as the percentages found in the group consisting of full remissions only;

and these two groups together, as already stated, present a sharp contrast in this respect to the group of patients who were essentially unimproved from the mental standpoint, even though the proportion in the latter group of those who exceeded their pretreatment weight is by no means insignificant.

The maximum gain was attained in the neighborhood of six months subsequent to the completion of treatment. This advance averaged 10 pounds (4.5 Kg.) at three months (sixty-two cases), and 13½ pounds (6.1 Kg.) at six months (forty-seven cases)—a net average increase of 8 per cent and of 10.5 per cent, respectively, of the "original" weight. It is of interest that the average gains for the three groups of patients showing various degrees of mental improvement not only are in dis-

TABLE 5.—*Percentage of Maximum and Minimum Changes in Pretreatment Weight* *

		4 Weeks	8 Weeks	3 Months	6 Months
Good remissions	Minimum	−10.3	− 8.1	− 3.0	− 2.1
	Maximum	+14.3	+19.9	+28.7	+32.6
		(22 cases)	(22 cases)	(22 cases)	(17 cases)
Moderate remissions	Minimum	− 8.6	− 8.0	+ 1.0	+ 6.7
	Maximum	+11.2	+15.0	+16.8	+21.1
		(13 cases)	(13 cases)	(13 cases)	(10 cases)
Slightly improved	Minimum	− 2.6	− 1.9	− 1.9	+ 0.8
	Maximum	+ 5.1	+11.3	+19.0	+31.4
		(7 cases)	(7 cases)	(7 cases)	(6 cases)
Unimproved	Minimum	−14.4	− 7.3	−10.6	− 5.6
	Maximum	+ 4.2	+11.2	+15.6	+17.9
		(15 cases)	(15 cases)	(15 cases)	(11 cases)
Worse	Minimum	− 9.7	−10.3	−14.3	−16.4
	Maximum	+ 4.2	+ 6.3	+ 1.4	− 2.9
		(5 cases)	(5 cases)	(5 cases)	(3 cases)

* It should be noted that although the minimum values (which are almost always a weight below the pretreatment level) have no discoverable relationship to each other, the maximum percentage gains vary almost uniformly in direct relation to the mental condition, and this is rather more conspicuously so in the early periods (4 weeks and 8 weeks).

tinctly close agreement among themselves but, when considered together as a single group of "improved" cases, are differentiated very clearly from the group of cases showing no appreciable mental improvement (tables 3 and 4, and chart 5).

Table 4, giving the data of table 3 computed in terms of the percentage of pretreatment weight gained by each patient, presents the situation with greater accuracy than do the weights themselves for the obvious reason that a gain of 10 pounds, for example, is significant chiefly in relation to the weight of which it is an increment, and has a different import in a man weighing 125 pounds (57 Kg.) from what it has in one weighing 190 pounds (86 Kg.). The pretreatment weight of the patients in this series ranged from 95 pounds (43 Kg.) to 207 pounds (94 Kg.) The great majority weighed from 135 to 150 pounds (61 to 68 Kg.) immediately prior to treatment. The average pretreatment weight for the total group of sixty-two patients was 142.1 pounds (64.6 Kg.).

As a second observation we have, then, the fact that the amount of the advance over the pretreatment weight is extremely variable, extending from zero or below to 32 per cent.

With regard to the subsequent maintenance of the maximum weight gained, it will be observed that the net advance registered at six months by the patients with full remissions, and by the "improved" cases as a

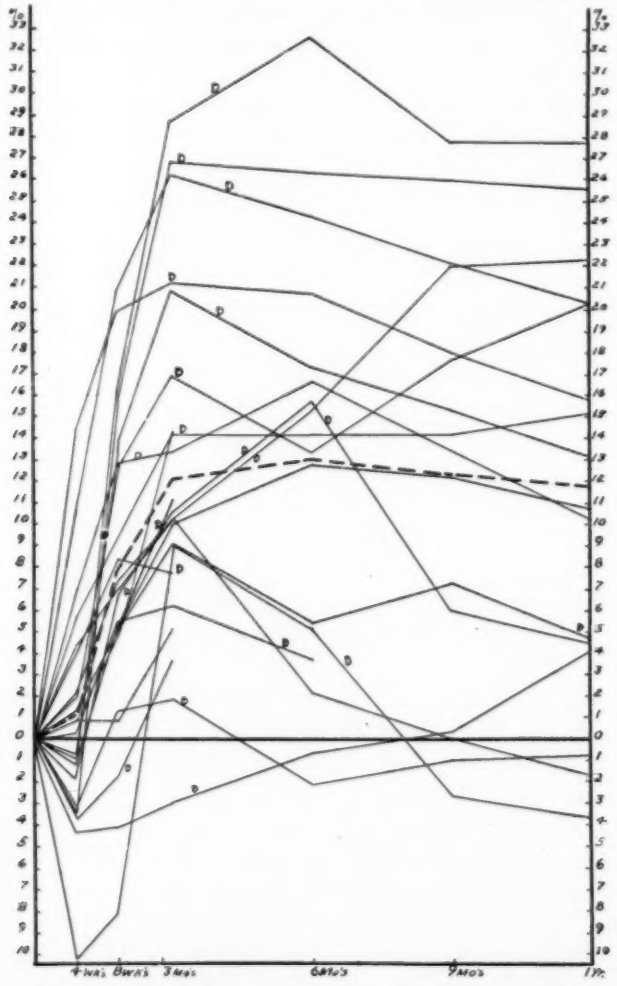

Chart 1.—Individual weight curves of the group of full remissions (plotted as percentage increments of the pretreatment weight); *D* indicates date of discharge from the hospital; broken line, average of total group.

whole, is fairly well sustained through the succeeding six months; while the slight tendency of the net gain in weight to become diminished during this latter period for the entire group is due almost wholly to the influence of the "unimproved" cases, in which there was an average loss

of 7½ pounds (3.4 Kg.) from the maximum attained at six months. It may also be noted that the patients with full remissions were somewhat less successful in maintaining the maximum gain than were the "improved" patients who fell short of complete remissions.[3] The difference in this respect between the examples of full remissions and the group of only moderately improved cases is due in some part, perhaps, to the smaller number of cases included in the latter, but it probably arises principally from the fact that the moderately improved patients have almost all remained in the hospital in relative physical inactivity, whereas the patients who attained complete remissions have been at home and gainfully employed for considerable periods—in most instances in excess of a year. Our material makes it appear likely that the maximum weight which these patients reached at the end of from three to six months represents, in many instances, a condition of overweight, which in the case of those patients who returned to their former occupations became sooner or later reduced to what has in many instances been ascertained to be approximately the habitual weight prior to the onset of the illness. This may likewise be the explanation why some of the much improved patients showed a still further diminution, at the end of one and one-half years, of the amount of weight by which they had earlier exceeded their pretreatment level; although half of the patients followed throughout the longer period still weighed at the end of eighteen months from 12 to 29 pounds (5.9 to 13.2 Kg.) more than they did prior to treatment (tables 3 and 4).

The third principal fact which the present material seems to demonstrate is that after the maximum increase above the pretreatment weight level has been reached (at the end of not more than from three to six months), there takes place in an appreciable proportion of cases a diminution in this increase which extends in a gradual manner over the succeeding six months or longer. This is most marked among the patients who have remained mentally unimproved (table 3 and chart 3), as though a suppositious "malaria effect," slight at best in these cases, had soon exhausted itself. The tendency to decline is also somewhat definitely present among the patients who have achieved full remissions and have returned to work—as though they had earlier reached in many instances a condition of overweight which became gradually rectified under the influence of a return to their normal mode of living (table 3 and chart 1). On the other hand, the decline is little in evidence among

3. Of the sixteen patients to attain full remissions, three showed at the end of a year from the completion of treatment no material reduction of their maximum gain, and three even registered a further increase over their pretreatment weight; but the remaining ten fell off from 4½ to 17 pounds (2.0 to 7.7 Kg.), or from 2.5 to 12.5 per cent of their pretreatment weight, from the maximum which they had previously reached, although only three of these ten actually fell below their pretreatment level, and this by quite insignificant amounts (chart 1).

the moderately improved patients, whose continued stay in the hospital has very possibly done something to favor the state of overnutrition which the maximum degree of advance over the pretreatment weight perhaps in many cases represents (table 3 and chart 2).

If this accounts to some degree for the gradual reduction of the earlier gain which many of these patients eventually manifested, it is less

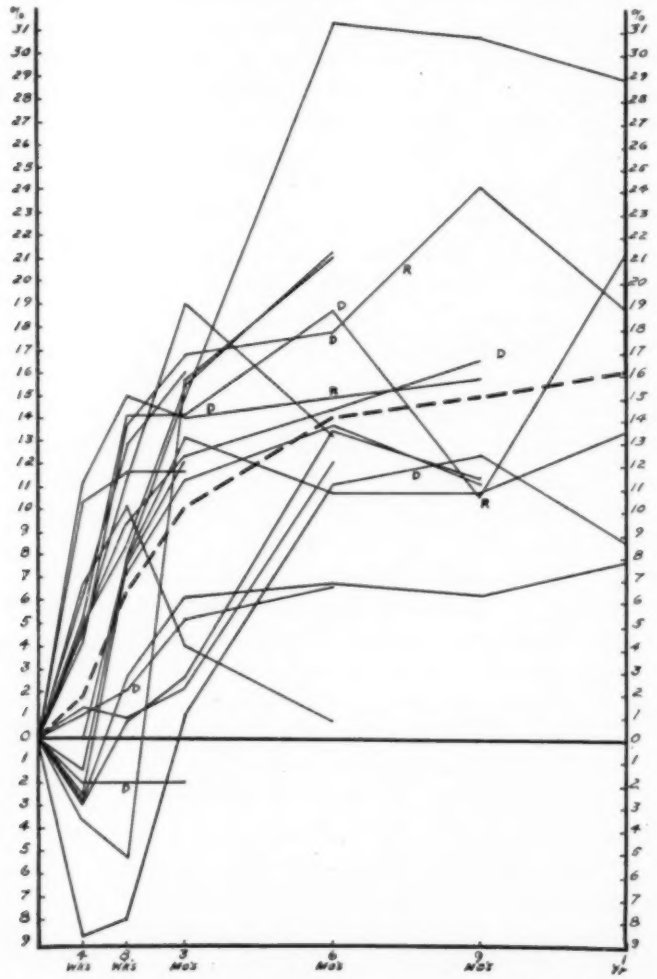

Chart 2.—Individual weight curves of the group of moderately improved and slightly improved cases; *D* indicates date of discharge from hospital; *R*, date of return to hospital; broken line, average of total group.

easy to evaluate the original advance in weight which carried many of them so far above the level at which they stood when treatment was first instituted. We have seen that this advance is not correlated, except in the most partial way, with the presence of mental improvement fol-

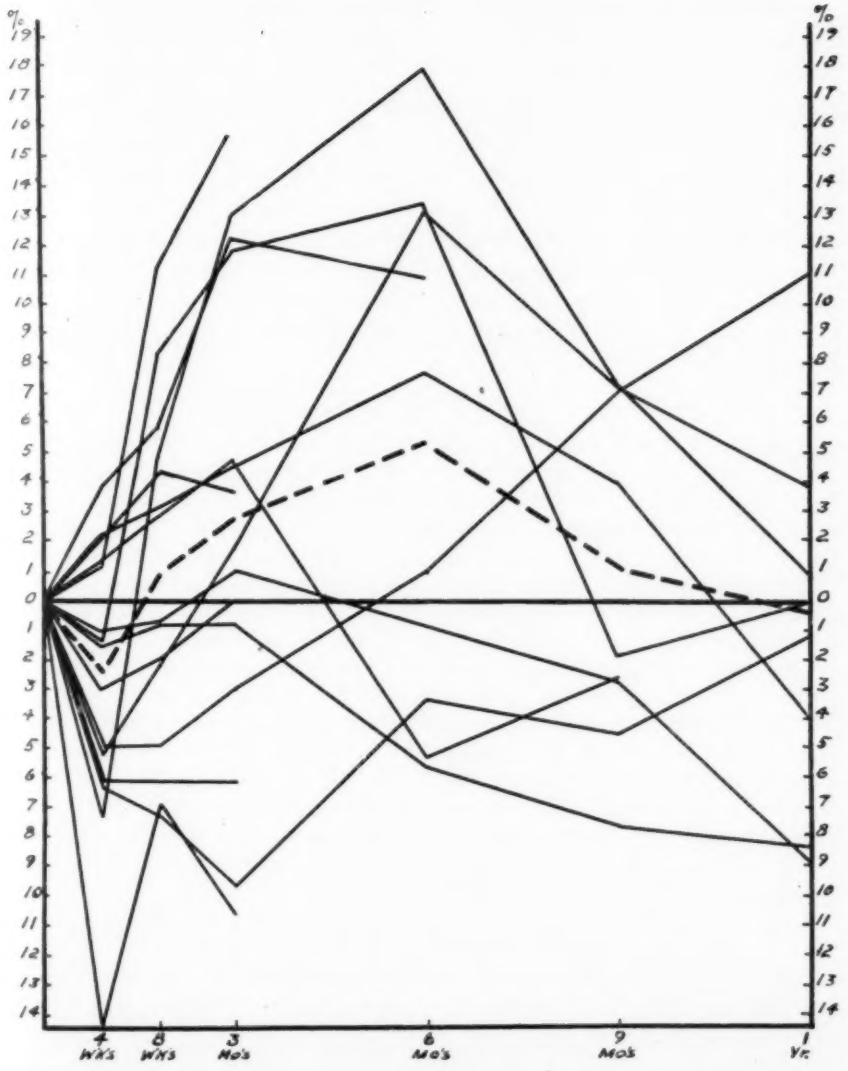

Chart 3.—Individual weight curves of the group of unimproved cases; broken line indicates average of total group.

lowing treatment, still less with the degree of that improvement. Does it depend, rather, on a condition of underweight at the time treatment was instituted? We know that such a condition is fairly common in patients with general paralysis.[4] Unfortunately, it has often not been possible to obtain accurately the customary weight of these patients in health, so that the actual amount of weight which they have lost, even when this is definitely known to have occurred, cannot be more than roughly estimated. Hence it is difficult to say whether or not a material gain in weight following malaria treatment is conditioned by a preceding loss, and particularly to know to what extent the maximum post-treatment weight attained, or for that matter the lower level which may subsequently be reached, represents an actual excess over the "normal" value for the patient. In the following cases the data are accurate enough to demonstrate a certain trend in this respect—a trend which might conceivably characterize the greater number of the patients in this series.

REPORT OF CASES

Case 1.—H. T. M., a man of large frame and excellent muscular development, weighed 191 pounds (87 Kg.) on admission to the ward. There was no evidence from any source that any loss of weight had taken place. During the five months which elapsed before malaria treatment was undertaken he lost 19 pounds (8.6 Kg.). Four weeks after the final malarial paroxysm he had made up the 10 pounds (4.5 Kg.) lost during the course of malaria and had gained 12 pounds (5.4 Kg.) in addition. At the end of eight weeks from the completion of treatment the gain had increased to 22 pounds (10.0 Kg.); at the end of three months his weight was not only 23 pounds (10.5 Kg.) in excess of his pretreatment weight, but was 4 pounds (1.8 Kg.) above his (normal?) admission weight. At this time he was discharged from the hospital. Three months later—six months after completion of treatment—he weighed 28½ pounds (12.9 Kg.) more than he had immediately prior to malarial inoculation. At the end of a year, however, this excess had fallen to 17½ pounds (7.9 Kg.), and at the end of one and one-half years from his final attack of malaria it amounted to 18½ pounds (8.4 Kg.), just one-half pound (0.2 Kg.) short of his admission weight of 191 pounds, which was presumably his normal weight in health.

Case 2.—H. A. L. weighed 136 pounds (62.5 Kg.) on admission, and 133 pounds (61.0 Kg.) three weeks later, immediately prior to inoculation with malaria. Even from an unusually intelligent informant it was impossible to learn that any loss of weight had taken place prior to admission. Four weeks after the completion of treatment this patient weighed 19 pounds (8.6 Kg.) more than he had just prior to inoculation; at the end of eight weeks this advance amounted to 26½ pounds (12.0 Kg.); at the end of three months to 28 pounds (12.7 Kg.). He was then discharged from the hospital, and at the end of six months the gain was still 28 pounds. At nine months, however, this excess had been reduced to 24 pounds (10.9 Kg.), and at the end of a year to 21 pounds (9.5 Kg.). At the end of one and one-half years he weighed only 13 pounds

4. Bunker, H. A., Jr.: Loss of Weight: Its Importance as an Early Symptom in General Paralysis, Arch. Neurol. & Psychiat. **15**:63 (July) 1926.

(6.0 Kg.) more than he had when treatment was commenced; but on the other hand, this weight of 146 pounds (66 Kg.), as it was then possible to learn from the patient, was a close approximation to his normal weight in health.

Case 3.—J. B. E., a distinctly corpulent person, weighed 188 pounds (85.5 Kg.) on admission, and 191 pounds (87 Kg.) two weeks later, just prior to inoculation. It was reasonably certain that no loss of weight had occurred prior to the institu-

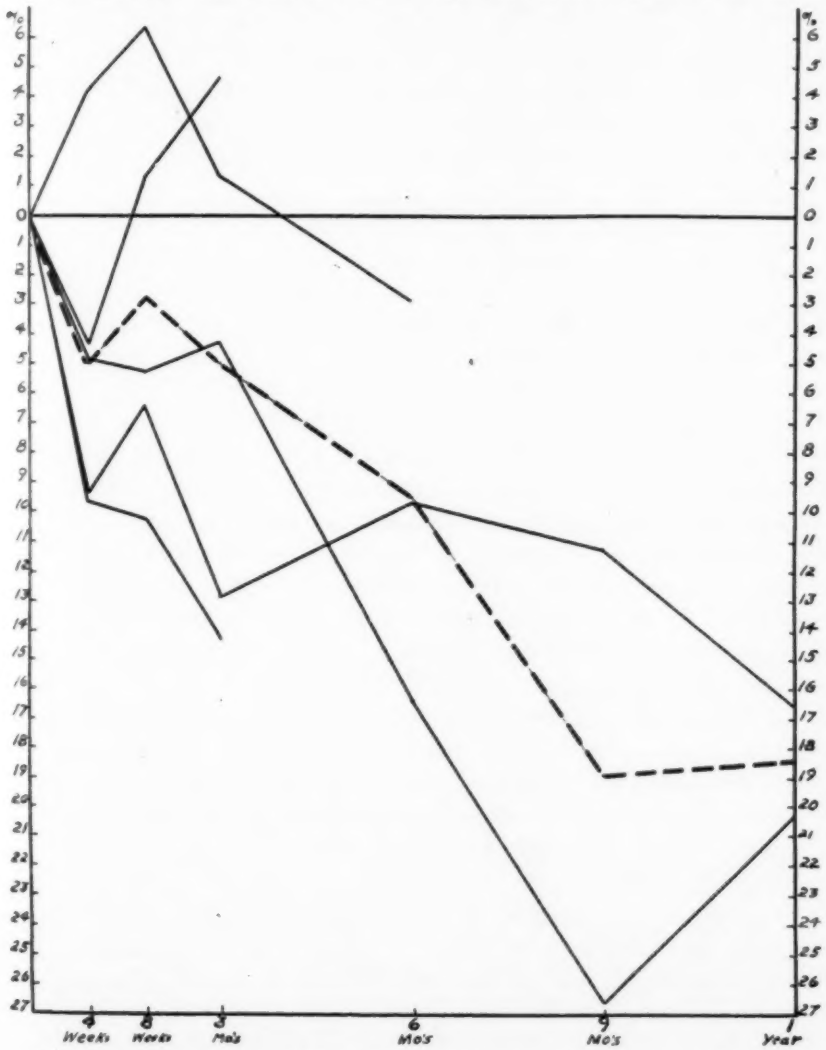

Chart 4.—Individual weight curves of patients worse or dead; broken line indicates average of total group.

tion of treatment. During the course of malaria he lost the rather unusual amount of 12 pounds (5.4 Kg.), and at the end of four weeks he was 6 pounds (2.7 Kg.) short of making up this loss. At the end of eight weeks he weighed 2½ pounds (1.1 Kg.), and at three months 3½ pounds (1.6 Kg.) more than he had before treatment was begun; this latter, however, was the maximum advance

over his initial status. At this time he was discharged from the hospital. At the end of a year he was 2 pounds (0.9 Kg.) under his pretreatment weight, and at the end of one and one-half years the deficit amounted to 5 pounds (2.3 Kg.). This, however, represents but 2.5 per cent of the pretreatment weight, and moreover, at 186 pounds (84.5 Kg.), is in essential agreement with his admission weight (188 pounds) and his usual weight in health.

The last patient, who gained no weight subsequent to treatment, attained a clinical remission fully as complete as did the other two, who gained weight apparently in virtue of a preceding weight loss which had taken place in the one case during the prodromal period of the disease, in the other only subsequent to admission to the hospital.

COMMENT

Whether or not posttreatment gain in weight of more or less conspicuous character takes place only on the basis of a preceding loss of material degree, there is no question that the maximum gain in weight achieved during the first three to six months of the posttreatment period represents a level, in at least a certain number of cases, well above the normal weight in health, and above the level which most of these patients are subsequently able to maintain (charts 1, 2, 3 and 4). In view, then, of the often temporary character of the weight increase and of its tendency not infrequently to overcompensate a preceding loss (to say nothing of its occurrence in numerous patients who exhibit no benefit in the mental sphere from the treatment), is it not possible that the gain in weight is a phenomenon inherent in the malaria treatment itself—an integral part of the reaction of the patient to that form of therapy, although perhaps a phase of that reaction which in some cases comes to expression only when the patient's weight at the time of undergoing treatment is below its ordinary "normal" level? Indeed, a similar gain in weight has long been recognized as not infrequently accompanying other forms of foreign protein therapy.[5] One calls to mind the experience of Uddgren,[6] who made this observation in detail in connection with the use of milk injections; and it should not be overlooked that from the clinic of von Wagner himself has come a description of the definite posttreatment gain in weight which took place in a miscellaneous group of mental patients who received injections of tuberculin and of pyocyaneus

5. That the malaria treatment is virtually a form of foreign protein therapy is perhaps not proved; but one may admit the outward similarity between the two with respect to the initial chill, the sudden brief pyrexia of considerable degree, the gradual defervescence with often profuse sweating and the behavior of the leukocyte count, which I have studied.

6. Uddgren, G.: Einige Erfahrungen über die therapeutische und diagnostische Bedeutung der Milchinjektionen, besonders in der Ophthalmologie, Stockholm, I. Haeggström, 1918, pp. 121 and 122.

vaccine.[7] Nor is it without interest in this connection that, according to Butomo,[8] a favorable prognosis attended those patients who reacted to protein treatment with a lowering of the elimination of nitrogen and phosphates, whereas the opposite was true of those in whom this elimination was enhanced.

It would seem justifiable to suppose, then, that gain in weight, as reported here in connection with the malaria treatment of general paralysis, is a manifestation which the treatment per se is potentially

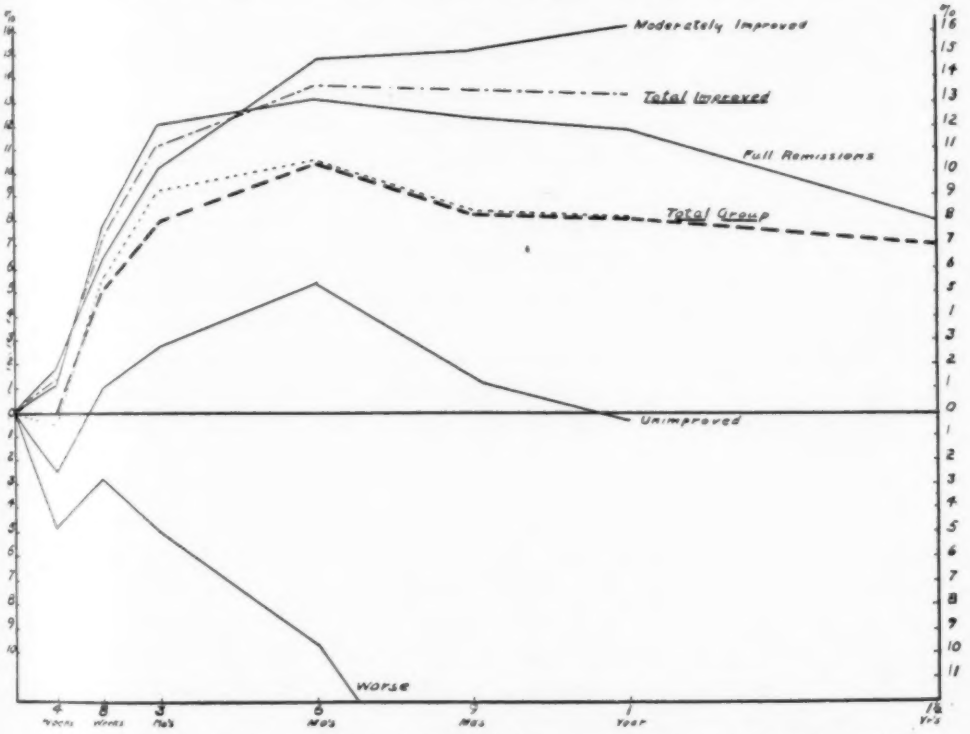

Chart 5.—Averages for the four clinical groups, and average for the total series; dotted line indicates group of cases (33) followed throughout one year; all other curves represent total group.

capable of eliciting in all patients subjected to it. When a definite gain in weight fails to take place during the first three months after the completion of the course of fever, it may be because the patient was more or less completely refractory, for reasons as yet obscure, to therapy

7. Boeck, E.: Versuche über die Einwirkung künstlich erzeugten Fiebers bei Psychosen, Jahrb. f. Psychiat. **14**:199, 1896.

8. Butomo, W.: Einige Angaben über den Stoffwechsel des gesunden und kranken Organismus bei parenteralen Milchinjektionen, Arch. f. Gynäk. **126**:291 (Oct.) 1925.

of this type; something of this kind is suggested by the fact that those patients who exhibit no response whatever, from the standpoint of mental improvement, in many instances gain little weight or none at all (charts 3, 4 and 5). But when material gain in weight does take place within the period indicated, the degree to which it is accompanied by mental improvement, temporary or permanent, will quite naturally depend on other and extratherapeutic factors, such as the presence or absence of organic damage beyond the possibility of functional restitution. Some such view would seem to be suggested by the similarity of the weight curves earlier referred to between the only moderately improved and the much improved cases, and the marked contrast which in general these offer to the patients in the wholly unimproved group.

Regarding the prognostic significance of the behavior of the weight curve in the individual patient, it is safe to say that actual loss of weight, or even partial or complete failure to make up the loss sustained during the course of malaria during the first three months of the posttreatment period, is an unfavorable indication. But to even a well marked gain in weight cannot unqualifiedly be attributed a favorable significance (charts 2, 3 and 4). Although in following the individual weight charts from week to week one cannot fail to be struck by the frequency with which a decided gain in weight is completely synchronous with definite mental improvement, the fact remains that this response is in some cases temporary; in others, extraneous factors may preclude a therapeutic result on the mental side.

The gain in weight here considered is chiefly significant in its suggestion of a rather fundamental alteration in the organism resulting from the malaria treatment. It is the most visible, whether or not the most profound, of the various only partially determined humoral changes which underlie the altered reactivity of the organism (*Umstimmung*) such as is believed to come about in patients who respond therapeutically to nonspecific foreign protein treatment.[9]

SUMMARY

1. In a series of malaria-treated cases of general paralysis, a gain in weight above the pretreatment level took place during the first three months subsequent to treatment in 80 per cent of the sixty-two patients. Such an advance was found in about 50 per cent of the mentally unimproved cases; but it occurred in 95 per cent of the patients who achieved full remissions, and of those who showed more moderate mental improvement.

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9. Bunker, H. A., Jr., and Kirby, G. H.: The Treatment of General Paralysis by Inoculation with Malaria: A Second Report, Arch. Neurol. & Psychiat. **16:** (Aug.) 1926.

2. The increase in weight averaged 13.4 pounds (6.1 Kg.) at the end of six months, when the peak value was reached, an average advance of 10.3 per cent of the pretreatment weight. At this time the eleven mentally unimproved patients averaged only 6.9 pounds (3.1 Kg.) more. The thirty-three improved patients, on the other hand, gained weight practically irrespective of the degree of mental improvement, the gain averaging 18.5 pounds (8.4 Kg.), an advance of 13.7 per cent of the pretreatment weight.

3. From the point of maximum gain at the end of six months, a certain tendency to decline was evident through the next six months. In the thirty-three patients followed for a year, this reduction was from an average gain of 13.9 pounds (6.3 Kg.) to 10.3 pounds (4.7 Kg.). For this decline the "unimproved" cases were largely responsible.

4. Failure to recover part or all of the weight lost during the actual course of the malarial infection seems definitely to be of unfavorable prognostic significance. On the other hand, a marked and rapid rise of the posttreatment weight curve above the pretreatment level is often exactly coincident with well marked mental improvement, and is of favorable prognosis up to a certain point; but this improvement is sometimes only temporary, and even in the presence of a maximum response from the standpoint of weight increase, a maximum result as regards the mental outcome may be prevented by the presence of other factors, such as organic damage beyond the possibility of functional restitution.

5. The posttreatment gain in weight is probably more or less intimately connected with the mechanism of the malaria therapy itself as suggested by the facts that: (1) many patients exhibit it who show no mental improvement; (2) the maximum weight reached is not infrequently considerably in excess of the usual weight in health; (3) the maximum gain is often only temporary, and (4) a similar phenomenon has been observed in connection with foreign protein therapy of other types.

6. The principal significance of the gain in weight here described consists in the suggestion of a fundamental alteration in the vital processes of the organism (*Umstimmung*), which in some obscure way underlies the striking therapeutic results following malaria treatment.

Clinical and Occasional Notes

AN ENCEPHALITIC RESIDUAL SIMULATING PROGRESSIVE MUSCULAR ATROPHY OF SHOULDER GIRDLE TYPE

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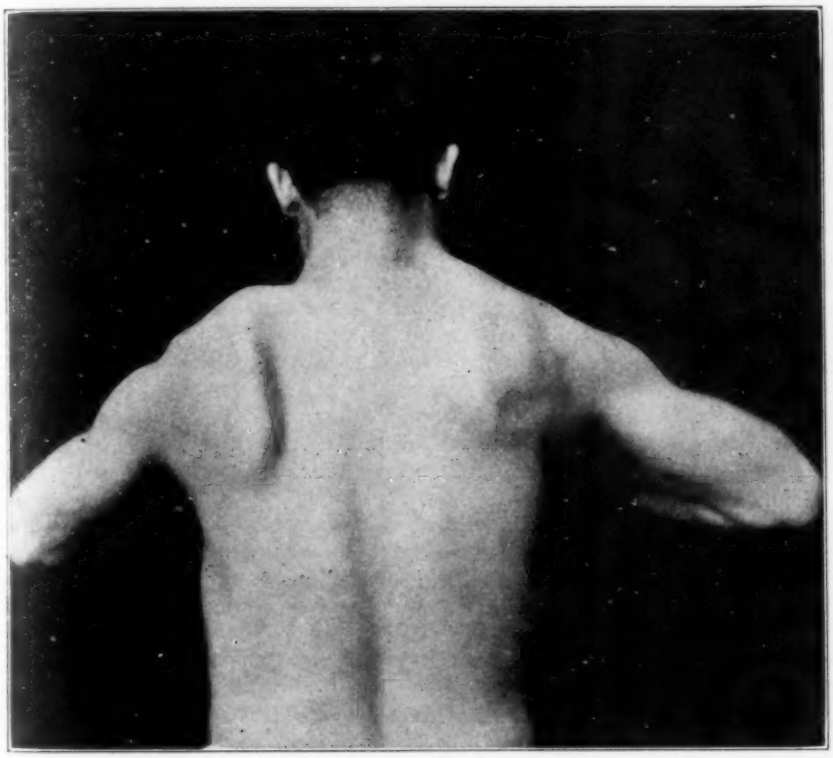
The etiology of primary progressive muscular atrophy is unknown. Exposure to cold, overexertion, fatigue, trauma, toxins and infections, and hereditary and familial tendencies have been mentioned. Gowers[1] believed that some nervous diseases, particularly of the motor system, were due to systemic degeneration of nerve elements which have a common function. He devised the term abiotrophy to describe them and gave Friedreich's disease as a typical illustration. Spiller[2] has called attention to the presence of syphilis as an etiologic factor in a certain small percentage of cases of progressive muscular atrophy. In the report of the Association for Research in Nervous and Mental Diseases on acute epidemic encephalitis,[3] 1921, mention is made that "either the spinal or bulbar form of progressive muscular atrophy may sometimes be simulated by the more subacute forms of epidemic encephalitis." Grinker[4] refers to a case, which he regards as a combination of acute anterior poliomyelitis and epidemic encephalitis, in which there was atrophy of the muscles of the left forearm and hand of the Aran-Duchenne type. Fromment and Gennevois[5] describe a case of encephalitis with Aran-Duchenne atrophy of the right hand and forearm, with later development of spastic paresis of the right leg. Lhermitte[6] discusses the various types of muscle atrophies in encephalitis but makes no mention of a pure progressive muscular atrophy syndrome. Souques and Alajananine[7] report a case of progressive muscular atrophy starting in the arms, extending to the legs and finally resulting in bulbar death. Necropsy showed lesions of an extensive poliomyelitis. Experimental attempts to reproduce the disease in guinea-pigs and rabbits by intracerebral inoculation of emulsions of the cord were successful.

REPORT OF CASE

Clinical History.—The patient, an Italian, a coal miner, aged 29, entered Barnes Hospital, Oct. 19, 1925, in the service of Dr. S. I. Schwab, complaining of headache, dizziness, weakness and trembling. He was born in Italy in 1896, came to the United States at the age of 15, and worked as a bricklayer for several years, and then as a coal miner until he entered the army. During the epidemic of 1918, he had an acute illness diagnosed as influenza which was

1. Gowers: Clinical Lectures, Philadelphia, P. Blakiston's Son & Co., 1904.
2. Spiller, W. G.: J. Nerv. & Ment. Dis. **39**:584, 1912.
3. Report of Association for Research in Nervous and Mental Diseases on Acute Encephalitis, New York, Paul B. Hoeber, 1921.
4. Grinker, Julius: J. Nerv. & Ment. Dis. **111**:323 (Oct.) 1920.
5. Fromment and Gennevois: Rev. neurol. **28**, 1921.
6. Lhermitte, J.: La Médicine **5**:354, 1923-1924.
7. Souques and Alajananine: Ann. de méd. **15**:281, 1924.

characterized by generalized pain, fever, cough and diplopia. He was delirious during the first four days. After several weeks he returned to duty, and in drilling noticed that he was nervous and weak. After discharge from the army in February, 1919, he resumed mining, but was unable to work more than a day or two at a time. In May, 1921, he finally stopped all work on account of weakness. About this time he complained of sore muscles, somnolence, periods of diplopia and, on one occasion, loss of consciousness. By 1923, weakness of the arms had increased to such a degree that he could not raise them above his shoulders. During March, 1924, he had a period of confusion, inability to close his left eye and drawing of his face to the right. Since discharge



Winging of the scapula and deltoid atrophy.

from the army he has been hospitalized several times with no relief. There has been increasing weakness of the shoulders so that when admitted he was unable to raise his arms beyond a right angle.

Physical Examination.—Examination revealed a well developed, muscular man. He sat with the arms resting on the knees, and the shoulders drooping slightly forward. Marked bilateral depression and flattening of the anterior chest was noted. This was caused by almost complete atrophy of both pectoral groups of muscles. The second, third, fourth and fifth intercostal spaces were apparent with a ridge produced by the disappearance of the pectoralis major. The ridge and hollow were greater on the right than on the left. Both clavicles were very prominent with particular accentuation of the intraclavicular space

in relation to the upper part of the sternum. This part of the chest appeared as though it were caved in. The deltoid regions were atrophic, the curves over the shoulders flattened and pointed. The intrascapular region was flattened, and the lower ends of both scapulas stood out prominently from the chest wall. The supraspinous and infraspinous scapular regions were equally flattened, so that the whole outline of the scapulas was easily made out, as shown in the accompanying figure. The erector spinae muscles were flattened, particularly in the upper dorsal and cervical regions. From time to time fibrillary twitching was noted in the atrophic muscles, especially in the pectorals. Both shoulders tended to fall downward and inward. The muscular contour of the arms outside the shoulder girdle was normal, and all movements other than those of the shoulder girdle were carried out normally. The extended arm could be pulled across the abdomen, though with lessened power; this movement was accomplished by the upper fibers of the pectorals which were not as yet involved. The movement corresponding to this posteriorly, carried out by the latissimus dorsi muscles, was apparently not affected. Lateral abduction from the side of the body was only partially carried out, the arm coming to rest 30 degrees from the right angle; movement beyond this could not be carried out. The extended arm could be brought forward in a plane parallel to the floor but could not be raised above this. The extended arm could be carried backward only to a minimal distance. When both arms were abducted from the sides of the body, winging of the scapulas caused by weakness of the serrati muscles was observed. Owing to the impossibility of fixing the scapulas, the deltoids were unable to function in raising the arms above the right angle. In all these movements overaction of the trapezii occurred in the attempt to support the functions of the paralyzed group. The deltoids, pectorales major and minor, infraspinati, rhomboids major and minor, levator scapulae and serrati all showed atrophy, with loss of galvanic and faradic excitability. The latissimus dorsi and trapezius muscles responded normally to galvanic and faradic stimulation.

The pupils were equal and regular, and reacted normally to light and in accommodation. The fundi were normal. The external ocular movements were synchronous and intact, except for slight weakness of the left internal rectus muscle. There was slight asymmetry of the face, a residual of an old left facial paresis. The tongue was protruded in the midline without tremor. The biceps and triceps reflexes were equal and active. The knee and ankle jerks were equal on the two sides and active. The abdominal and cremasteric reflexes were present. There were no ankle or patellar clonus, and no pathologic toe signs. There was slight rigidity of the arms on passive manipulation, and this rigidity was also present to a slight degree in the legs. The gait was uncertain with a wide base. Superficial and deep sensation was everywhere intact.

Aside from signs of chronic bronchitis, the general physical examination gave entirely negative results. The blood and spinal fluid Wassermann reactions were negative. The red blood count was 5,800,000; white blood count, 8,000; hemoglobin, 88 per cent; stained smears of the blood were entirely normal. The urine gave negative findings.

COMMENT

This case is presented primarily with the view of recording it as an example of progressive muscular atrophy occurring during the course of epidemic encephalitis. It is of particular interest from an etiologic point of view. Such a process as occurs in epidemic encephalitis may well account for the occurrence of some of the more obscure progressive muscular atrophies.

News and Comment

FELLOWSHIPS IN NEUROPSYCHIATRY

Announcement is hereby made of the following appointments to the four fellowships in neuropsychiatry provided jointly by the Commonwealth Fund of New York and the Graduate School of Medicine of the University of Pennsylvania, for the three year period beginning Oct. 11, 1926, and at stipends of from $2,000 to $2,200 per annum: Dr. William G. Ferguson, Ann Arbor, Mich.; Dr. Alberta Jenkins, Indianapolis; Dr. Norvelle C. LaMar, Indianapolis; Dr. Raymond W. Waggoner, Philadelphia.

RESEARCH ON SLEEP

In 1924 the Simmons Fellowship was founded at Mellon Institute of Industrial Research, University of Pittsburgh, to carry on a broad study of problems in the promotion and maintenance of healthful sleep. Dr. H. M. Johnson and Mr. G. E. Weigand, psychologists, and Dr. T. H. Swan, physical chemist, have been conducting this research during the past year. Recently, Dr. Carney Landis, physiologist, has temporarily joined the personnel of the investigation. It is announced that from now on there will be two separate Simmons Fellowships at Mellon Institute. One of them will continue the research on the physiologic and psychologic factors of sleep under the supervision of Dr. Johnson. The other fellowship, held by Dr. Swan, will be concerned chiefly with the subject of bedding materials. This investigational work is being supported primarily for the benefit of the public and consequently the experimental results will be published.

Abstracts from Current Literature

TUBERCULOSIS OF MAMMALIAN TISSUE IN CULTURE. A. A. MAXIMOW, Ann. d'anat. path. et d'anat. norm. **3**:1-39, 1926.

"The method of tissue culture allows the reproduction of the essential phases of the tuberculous process under artificial conditions. It is possible in this way to follow the histogenesis of the lesions in the living state as well as in fixed and stained preparations, in all its stages and details, and to determine the origin of all the specific elements. The employment of this method in the study of the biologic relationships between tissue and bacillus under varied conditions seems to be indicated." These are Maximow's conclusions. His findings in summary are sufficiently clear and important to be given in his own words.

"From what has gone before it seems that when mammalian tissues and Koch bacilli are cultured together in vitro under favorable conditions, there is neither degeneration nor death of cells such as takes place due to saprophytic contamination, but rather a symbiosis. The two elements may grow and proliferate for as long a time as three weeks; at times isolated cells, living, and even in the process of division may be found within masses of the micro-organisms.

"Due to the presence of the Koch bacilli the tissue elements undergo a series of definite and specific reactive changes. The ensemble of phenomena observed in vitro is identical with the tuberculous process observed in the living organism including caseation; sometimes there is even a tendency to healing by invasion of the necrotic foci by fibroblasts.

"In lymphoid tissue the reticular cells are the most active elements. Just as in infected lymph nodes in the organism, they are mobilized, become active, divide and become transformed into large polyblasts and epithelioid cells, which phagocytose the bacilli. One of the most remarkable changes in these cells is the hypertrophy of the cytocenter. The epithelioid cells collect in masses corresponding to tubercles which, according to the terminology of Ivest and Emshoff, might be termed primitive tubercles. Numbers of these cells fuse, apparently by reduction in the surface tension of their protoplasm, and give rise to giant cells of the Langhans type. The increase in the number of nuclei is, in part, the result of amitosis.

"The lymphocytes, as in ordinary inflammation, also play an active rôle. They undergo hypertrophy and transformation into polyblasts, later may take on an epithelioid character and contribute along with the reticular cells to the formation of tubercles and giant cells. Rarely some bacilli may penetrate into the lymphocytes. Later, when these lymphocytes have become epithelioid cells, they phagocytose them actively.

"The bacilli taken up by the epithelioid cells are either digested, leaving a yellow (lipochrome) pigment, or proliferate abundantly, even outweighing the protoplasmic mass. The cells thus loaded with bacilli may preserve their vitality for a long time, move about and even divide by karyokinesis. The digestive power of giant cells is probably increased, because the number of bacilli in these cells is never excessive.

"The same end-results can be observed in tissue culture as in the experimental animal: caseation. In the large collections of cells, or in the tubercles, the epithelioid cells degenerate, with the appearance of numerous fine droplets,

accompanied by karyorrhexis and karyolysis. Finally, nothing is left but detritus with here and there some bacilli.

"Analogous features are observed in omental cultures and ordinary connective tissue cultures inoculated with Koch bacilli. In the former case the fixed cells are mobilized, becoming polyblasts and epithelioid cells, engulf the bacilli and form typical tubercles. In the latter, although the bacilli normally do not penetrate into the tissue, the migrating fixed cells hypertrophy, change into epithelioid cells, and small atypical giant cells arise by amitosis. Fibroblasts take no part in the formation of tubercles and giant cells, but remain separate from the other elements, although there may be an exception in the case of the omentum.

"The rôle of the endothelium in the production of typical tubercles is an important problem. Current or preponderant opinion, found in all pathologic treatises, says that the epithelioid and giant cells come directly from endothelial cells; and certain experiments seem to justify this view (Foot). But a more rigid examination of the facts and of the literature suggests that this opinion deserves careful revision. The problem depends on the definition of 'endothelium.' What is it that merits the name of endothelium?

"If this term is limited entirely to the flattened cells that cover the ordinary blood vessels, capillaries, arteries, veins and heart, and the lymphatic vessels, it would be difficult if not impossible to furnish proof of their participation in the production of elements constituting the tubercle. In tissue cultures as well as in inflammatory tissue prepared in the ordinary way it is easy to follow the transformations of this endothelium properly so called. The cells either preserve their tubular arrangement and produce new capillary branches, or change into ordinary strands of common fibroblasts. This corresponds exactly with what I observed twenty-two years ago in simple aseptic inflammation; the proliferating endothelium of the capillary veins may produce fibroblasts, but never gives rise to migrating ameboid cells or polyblasts. The epithelioid cells as is well known belong to the group of polyblasts. Even in cases where the fibroblasts of endothelial origin take on an embryonal character under the chemical influence of Koch bacilli they remain distinctly separate from the epithelioid cells of reticular or lymphatic origin and play no part in the genesis of giant cells.

"Conditions are immediately changed if the definition of the word endothelium is enlarged to include all the flattened cells that line lymphatic or blood spaces, such as the cells that line the sinuses of the spleen, the Kupffer cells of the liver, the reticular cells that pave the sinuses of the lymph nodes, etc. If we adopt this point of view, the epithelioid cells and giant cells of tubercles in the animal must be interpreted as results of transformation of endothelium. We know that in the liver the tubercles are formed essentially by the Kupffer cells (Oppenheimer, Evans, Bowman and Winternitz), in lymph nodes by the reticular cells of the follicles and sinuses (Ivest and Emshoff). But it seems to me that this is an abuse of the word 'endothelium', and that it may induce error. The elements just mentioned differ greatly in both structure and function from the ordinary endothelium of the capillaries, arteries, veins, heart and lymphatics. Whereas this is intimately related to the fibroblast whose form it may easily take on, the flattened elements that line the spaces mentioned belong ontogenetically and functionally to the large family of migratory cells.

"Scattered through the whole body, the migratory cells which arise in the early stages of ontogenesis from the mesenchyme, appear in various modifications. One part remains free and active (the migratory cells of connec-

tive tissue); others change into fixed stable immobile elements, but preserve in the latent state the possibility of migration. To this last category normally quiescent, but potentially migratory and ameboid, belongs a whole series of elements described by different authors under different names. There are (1) the fixed migratory cells of Maximow or clasmatocytes of Ranvier in ordinary loose connective tissue; (2) the adventitial cells of Marchand, or rhagiocrine cells of Renaud, identical with the fixed migratory cells of Maximow in the ometum; (3) the reticular cells and sinus cells of lymph nodes, of the spleen, of bone marrow; (4) the cells of Kupffer in the liver, and finally perhaps also the cells lining the blood capillaries in certain other organs, for example, the suprarenals.

"Under stimulation of all kinds all these cells may be mobilized and transformed into free elements, function as active phagocytes and engulf vital dyes and other colloidal substances. It is for this reason that they have been called by Maximow, migratory fixed cells. They all have surprisingly varied potentialities and may proliferate and differentiate into other diverse forms. To call attention to this quality, I gave them (1902) in their free active stage in focal inflammations, the name of polyblasts.

"Goldmann and Tschaschin were the first to recognize that all these elements formed a single great group and that they had physiologic properties and evolutionary potentials of an identical character. Goldmann termed them 'cells of Pyrrhol'. Kiyono grouped them under the name histiocytes although this term signifies nothing but 'tissue cells'. Evans gave them the name of macrophages formerly employed by Metschnikoff. By many other authors the whole group, spread through many organs and tissues, is designated under the term 'reticulo-endothelial apparatus.'

"These fixed migratory cells or histiocytes in all their modifications in different organs and tissues—and not the common endothelial cells—are the most active elements in all inflammatory processes and particularly in tuberculosis. Under the influence of inflammation they are mobilized and furnish polyblasts. When the inflammation subsides, the polyblasts that are not destroyed or exhausted during the course of the disease return to their fixed condition. In the normal animal they—and not the common endothelial cells—are in all probability the endothelial leukocytes, the monocytes, of the circulating blood.

"It is natural that the lymphocytes should also play an active part in the same inflammatory processes, and join with the polyblasts of tissue origin. The study of the embryonic histogenesis of the blood and of the connective tissue shows that genetically they are closely related to the histiocytes of fixed migratory cells (Maximow, Alfejew). In the embryo many become normally quiescent in the late stages of gestation and become transformed into histiocytes or fixed migratory cells. The histiocytes, for example, the reticular cells of the hemopoietic organs, on the other hand may give rise to lymphocytes, and the same is true even in the adult animal. As I have observed recently, the reticular cells or histiocytes of lymphoid tissue may, under certain conditions, produce large lymphocytes, even in tissue cultures.

"Tubercle bacilli exert an influence on these cells—notably on the fixed migratory cells or histiocytes—by means of specific chemical substances. This action is shown in tissue cultures as stages when there is still no trace of disintegration of the bacterial bodies. Cells may be influenced at a distance even without coming in contact with the bacilli; it is impossible therefore to compare directly the influence exerted by the tubercle bacilli on the cells with that exercised by dead foreign bodies even of the same size and chemical

composition. Virchow and Baumgarten believed that this specific chemical stimulant of bacillary origin was the direct cause of the hypertrophy and of the cellular proliferation, whereas Weigert thought that the first effect was to damage the living substance of the cell, thus provoking its degeneration, this being followed secondarily by a reaction of progressive character. The facts observed in inoculated cultures bear out the former theory. The presence of a sufficient quantity, often very small, of bacilli in a culture provokes throughout the whole explant characteristic and definite changes especially in the fixed migratory cells. These consist in growth and hypertrophy affecting especially the nucleus and the cytocenter, and in the alteration in surface tension of the cytoplasm; karyokineses without traces of previous degeneration may often be the immediate result.

"Of all the tissue elements, the migratory fixed cells or histiocytes are the most sensitive, just as the lymphocytes that accompany them in their transformations. But the presence of tubercle bacilli seems in general to have a stimulating action on the vital substance of certain other cells. For example, under this influence fibroblasts and endothelial cells (properly so called) retain their activity for a much longer period than ordinarily, or even acquire embryonic properties; fat cells rapidly lose their fat; small lymphocytes hypertrophy and change with extraordinary facility into large lymphocytes, etc. In lymphoid tissue cultures without bacilli there ordinarily develops about the sixth day a delicate intercellular fibrillar tissue; in cultures inoculated with tubercle bacilli I have never found the smallest trace of it."

FREEMAN, Washington, D. C.

ALZHEIMER'S DISEASE. E. GRÜNTHAL, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**: 128, 1926.

In addition to the fundamental works of Alzheimer and Perusini on Alzheimer's disease we have the descriptions of Kraepelin and Startz. These have failed, however, to give a sytematic, clinico-histopathologic description of the process, and so Grünthal has collected a number of cases with this end in view. The author reports on fourteen brains of Alzheimer's disease, the largest number reported in the literature, since up to the present only twenty typical cases of this disease have been placed on record. Most of the cases were diagnosed clinically by Kraepelin.

Since some of the material dated back many years, only certain sections were available. With only two exceptions the following areas were studied in the brains: frontal (chiefly at the pole), cornu ammonis, the subiculum and the occipital cortex in the region of the area striata. Sections were stained by the methods of Nissl and Bielschowsky, and by a myelin sheath stain, Holzeir glia stain and Herxheimer's fat stain; often the methods of Klarfeld-Achucarro, Alzheimer-Mann, van Gieson, Levaditi and Jahnel were used.

Necropsy showed the following: general examinations in eight of the cases showed slight arteriosclerosis and arteriosclerotic kidneys in five cases; one case showed no sclerosis; two other cases showed coronary sclerosis, contracted kidneys, severe atheroma of the aorta and a severe peripheral sclerosis. The gross appearance of the brains was described in five cases. Three of these showed advanced atrophy of the frontal convolutions; in one the atrophy was most severe in the occipital region. In two cases the basal ganglia seemed smaller in size, the atrophy was intense, and the brain weight was 870 and 930 Gm., respectively. The fifth brain weighed 1,140 Gm., and showed no atrophy, swelling or edema.

Histologic studies in this series of cases revealed the so-called senile plaques in thirteen cases as well as the fibrillar changes of Alzheimer. This was observed in sections stained by Bielschowsky's method. In some cases the plaques were very few, while in others the entire cortex was saturated with plaques. Plaques were found only in the cortex, or at least in the most superficial part of the white matter, but for the most part in the cortex. In severe cases isolated plaques were found in the putamen. The cerebellum was entirely free. The location of the plaques in the cortex differed; many cases showed them in the second and third layers (Brodmann), but in the most severe cases they were scattered throughout the cortex. Similarly with the fibrillary changes. In some cases they were hard to find, while in others many cells in one focus were involved. Glia preparations showed the cortex saturated with fibers, especially in the middle and lower layers. As Alzheimer had pointed out, the fibers were extraordinarily thick in contrast to their fine quality in senile dementia. In six cases which showed only slight increase in glia the cornu ammonis was markedly sclerosed. Simchowicz demonstrated the same finding in senile dementia. Fat stains showed the fat somewhat increased in the nerve cells, in some cases occupying from one-half to two-thirds of the entire cell. The cells of the cornu ammonis were particularly rich in fat. Some cases showed no fat, while in most of the cases, fat droplets were found either in the adventitial or perivascular lymph spaces. Myelin sheath stains showed a diffuse disappearance of radial and tangential fibers, severe in nature. Nissl preparations showed an atrophy of the cortex with a disappearance of nerve cells, disturbance in architecture and increase in glia cells. Almost all the cases showed shrinking of the nerve cells, and a few showed chronic cell changes. In seven cases acute cell changes were present. Glia changes were most prominent in layer 1 (Brodmann), cell changes in layers 2 and 3. Hortega glia cells were found in the very severe cases. Arteriosclerotic changes were found in five cases in the form of slight intimal proliferation, and, in the basal vessels, hyaline changes in the media.

Grünthal attempts to correlate closely the clinical and pathologic findings in his series of cases. As to age, the majority of patients were between 52 and 63. This is presenile if one takes the presenile period as 50 to 65. Two cases fell outside this span, however, occurring at 47 and 67. O. Fischer reports a case of presenile dementia occurring at 70, and the possibility of Alzheimer's disease occurring during the senile period is well known. "The course of the disease is extraordinarily uniform." All thirteen cases were remarkably alike in regard to symptoms and clinical picture; Kraepelin speaks of the "Familienähnlichkeit" of these conditions.

The clinical course is divided into three stages: 1. The disease begins with gradual loss of memory and disturbance in perception. Carelessness in work and appearance develop at the same time. Often confusion in places well known to the patient is an early complaint. Weakness or epileptiform attacks often appear in the beginning, and finally, loss of words and slurring speech appear soon after the onset. 2. In this stage complete disorientation sets in. Patients do not recognize relatives and often cannot find their way home. At the same time, understanding of the use of words and handling become worse. Reading, writing and arithmetic are severely involved. Restlessness at night follows and, finally, confused wanderings by day. 3. In this period logoclonia is clearly developed. The patients show the characteristic extreme irritability, are unclean, and react to stimuli only with paraphasic, logoclonic fragments; they understand practically nothing. The sucking reflex is often present, and the expression and movements are stereotyped—as pulling, rubbing and shouting.

With this clinical conception one can divide cases of Alzheimer's disease into slight, medium and severe, and so attempt to correlate clinical and pathologic findings. To do this Grünthal made a quantitative study of plaques, fibrillar changes, fatty and glia changes, etc., in one slight case, five moderately severe cases, five severe cases and two cases which were transitional between the moderate and severe. He classified his changes quantitatively as plus 1, 2, 3 or 4, counted several fields, and from his studies concluded that the severity of the clinical pitcure was parallel with the severity of the pathologic picture. For example, the number of plaques in the brain was greatest in the severe cases, next in the transitional cases, less numerous in the moderate cases, and least of all in slight cases. The most severe fibrillary changes were found in the severe and transitional cases. The fatty changes were so diffuse and constant that one could hardly quantitate, but seemed more severe in the severe cases. Glia proliferation was most intense in eight cases in the cornu ammonis, and all were severe cases. Grünthal states that one can say that a plaque count greater than from 60 to 70 in a high power field speaks for a severe clinical case. The fibrillary and glia changes run hand in hand with the plaque formation.

The duration of the disease varies. The slight and moderate cases run from one and one-half to two and one-half years. The severe cases run one, three, five, eight and thirteen years, the most severe being the five year case, and the next the three year case. The course is therefore relatively slow and progressive, so that the slight and moderate cases have a short duration, and the severe cases a long duration. As to the distribution and localization of the process, it is worthy of note that basal ganglia and cerebellum were untouched. The distribution over the cortex is quite diffuse and the process always begins in the frontal lobe and subiculum.

Even with a typical clinical course outlined by Grünthal, and apparently a typical pathologic picture, the differential diagnosis is not always easy. Plaques occur in diseases other than Alzheimer's disease, for example, in senile dementia; Alzheimer found them in a tabetic patient, aged 30; Klarfeld in an epileptic patient, aged 46; Lafora in a carcinomatous patient, aged 61, and Simchowicz in schizophrenia. The presence of both clinical and pathologic pictures is necessary to establish a diagnosis of Alzheimer's disease. The occurrence of fibrillary changes in an early case of Alzheimer's disease, however, may serve to distinguish it from senile dementia, since plaques are common to both.

ALPERS, Philadelphia.

ERYTHREDEMA POLYNEURITIS. HARRY R. FOERSTER, Arch. Dermat. & Syph. **12**: 17 (July) 1925.

Erythredema, acrodynia, dermatopolyneuritis, chiropodalgia and "the pink disease" are some of the various names used to designate a peculiar disease of the nervous system, occurring in infants and young children, characterized by cutaneous manifestations of pathognomonic importance, and of which Foerster reports three cases. Acrodynia was the name applied originally to an epidemic cutaneous disease that appeared in France among poorly nourished inmates of asylums and among soldiers a few years after the first influenza pandemic. The disease the author discusses has a similar symptomatology, but occurs in infants and young children, is not characterized by epidemic occurrence, by food deficiences, or by intense pigmentation, and has been reported in several small series of cases in Australia, the United States and Canada, only within the last ten years.

As the earliest manifestation, the infant or young child shows a disinclination for food and resents any attempt to amuse it. These signs are accompanied, in many instances, by nasopharyngeal catarrh, which frequently subsides, to be followed by a quiescent period of from two to four weeks, during which the child seems well. With the onset of the signs of the disease the child becomes extremely wretched and irritable, and is sleepless. One of the first and cardinal symptoms is loss of appetite. A week or ten days after the onset the pathognomonic cutaneous signs appear. Profuse perspiration occurs, followed by a diffuse erythematous rash over the entire trunk and usually over the extremities. The fingers, toes, hands and feet become bright red, swollen, and cold, the redness being most intense distally. In many cases there is a similar condition of the ears, cheeks and the tip of the nose.

At the height of the disease the child will be found in a crouching position, with the extremities flexed on the trunk and its head buried in the pillow. The facial expression is one of great worry and concern and there is seldom a smile. There is photophobia ,and fretfulness and periods of dulness and apathy alternate with periods of constant restlessness. If the child is handled it will cry as if in pain. It scratches its trunk and extremities, particularly the latter, wrings its hands and even bites or gouges its hands and feet, so that extensive ulcerations may occur.

At the onset there is hyperesthesia and increase of reflexes; later, the reflexes become diminished or are lost, and there is diminished sensibility to pin prick. The muscles become soft and flabby and the ability to walk or even to sit up is lost. The teeth may be lost without any changes being apparent in the gums or alveoli; more rarely the nails are lost.

The pharynx and buccal mucosa are affected, the symptoms varying from a mild congestion to severe stomatitis with deep ulceration and sloughing of the soft any bony tissues. There is usually pronounced constipation. General adenopathy has been observed sufficiently often to be a diagnostic feature. The temperature is either normal or subnormal. The blood shows relative and absolute increase in polymorphonuclear leukocytes. Blood cultures have always been negative. Increased viscosity of the blood has been reported. The urine has shown frequently acetone and diacetic acid, and occasionally albumin. In most cases the cerebrospinal fluid is normal, but positive globulin reactions and positive reductions of Fehling's solution have been observed. The Wassermann reaction is always negative.

The author quotes the necropsy findings of Byfield and of Paterson and Greenfield. The former found spinal cord gliosis about the central canal, the ventral horn cells proximal to the anterior commissure showed poor staining qualities but the dorsal columns were normal. The sciatic nerve showed edema and swelling of the myelin sheath and edema of the connective tissue about the nerve fibers. There was no cellular infiltrate. Edema and swelling of the myelin sheath was seen also in the dorsal root fibers and in that portion of the nerve lying between the ganglion and the cord. Paterson and Greenfield report two cases that came to necropsy. In one the child was improving, but died from an intussusception; in the other, the child became steadily worse owing to a complicating generalized tuberculosis. In this latter case, the changes were at their maximum and proved conclusively that the disease is a polyneuritis affecting the peripheral parts of the nerve trunks. There was considerable myelin destruction in the peripheral nerves, increasing distally in degree and extent. In the central nervous system there was a diffuse increase of the small cells of the central gray matter, particularly in the lumbosacral enlargement.

In the motor cells of the ventral horns, especially in those supplying the distal portions of the limbs, there was moderate perinuclear chromatolysis, with eccentricity of the nucleus and the presence of large vacuoles in the cytoplasm. The increased cells in the nerve roots seemed to be derived from the cells of the nucleated sheath of Schwann, those in the spinal cord to be derived from the glia. The great increase of cells in the degenerated calf muscles appeared to be derived from the sarcolemma nuclei. Sections of the skin showed marked hyperkeratosis of the epidermis and pronounced edema of the collagen, with a moderate lymphocytic and fibroblastic infiltrate.

The disease is supposed to be due to an infection, and the toxemia, produced by the infecting organism, causes a sensory polyneuritis, chiefly of the peripheral parts, resulting in the peculiar syndrome of insomnia, anorexia, cutaneous irritability, vasomotor and trophic disturbances and dermatitis.

The treatment consists in forced feeding with a well balanced, highly nutritious diet, rich in vitamins, and in careful and intelligent nursing. For the skin, frequent, gentle cleansing and the application of sedative, antipruritic, emollient preparations and exposure to sunlight are indicated. Splints are necessary to prevent trauma from scratching.

The course of the disease is protracted, being usually from two to eight months, but in the absence of complications such as bronchopneumonia or septicemia, the prognosis is excellent.

PEARSON, Philadelphia.

COMPRESSION PARAPLEGIA DUE TO A VOLUMINOUS ANGIOCELE OF THE SPINAL DURA MATER. CONTRIBUTION TO THE STUDY OF MEDULLARY COMPRESSIONS DUE TO PATHOLOGIC VASCULAR PROCESSES. G. GUILLAIN and T. ALAJOUANINE, J. de neurol. et de psychiat. **11**:689 (Nov.) 1925.

One of the rarer causes of medullary compression of the cord is the circumscribed or diffuse pathologic development of the vessels of the pia mater or medulla. The aspects of this problem that have been best described are found in aneurysms of the spinal arteries and in angiomas. Varicose dilatation of the veins of the spinal pia mater is less well known, only twelve examples of this process appearing in the literature. This type of cord compression is produced by a diffuse vascular process, chiefly venous, asserting itself by huge dilatation of the vessels of the pia mater. The oldest observation is attributed to Gaupp (1887); this was followed by reports by Barenbruch (1890), Gerhardt (1895), Harman and Bolk (1900), Lorenz, Hadlich (1903), Raymond and Cestan (1904), Krause (1906), Jumentié and Levy-Voleusi (1911), Stanley Cobb (1915), Spiller and Frazier (1923), and Sargent (1925). The condition has been reported under numerous titles: cirsoid aneurysm (Raymond and Cestan), telangiectasis of the spinal cord (Spiller and Frazier), hemangioma of the pia mater (Sargent).

The case reported by Guillain and Alajouanine occurred in a soldier, aged 47, who showed progressive paresis of the lower extremities and then a spastic hemiplegia. The onset of the trouble had occurred in 1911, fourteen years previously, when the patient noticed from time to time that his left toe often struck the ground with great force, and that he stubbed his toe when climbing stairs. This trouble gradually increased over a period of two years and the patient tired while on the march. In 1914 pain appeared for the first time and was localized in the neck. The pain occurred every night, woke him from sleep, and disappeared completely after a few minutes on getting up. It was very

severe. The pains disappeared completely after two or three months and were followed by motor troubles, the paresis in the left leg by 1917 being quite noticeable. In 1918, pains in the neck of the same episodic character reappeared, and were followed shortly by vesical trouble in the form of retardation of micturition. In 1919 the patient experienced pains in the dorsal region. A diagnosis was made of compression due to Pott's disease and the patient was placed in a plaster cast for six months; the pains decreased, but the paresis of the lower extremities increased. In 1920, nine years after the onset, a spastic paraplegia developed with absolute loss of voluntary motion in the lower extremities, marked contractures and exaggerated automatic reflexes. These motor troubles remained the same until 1924. The tendon reflexes of the knee and ankle were greatly exaggerated, tapping often provoking an epileptoid trembling of the entire extremity; there was bilateral ankle and patellar clonus, a bilateral Babinski sign, and the cutaneous abdominal and cremasteric reflexes were absent. Sensory examination revealed complete loss of touch, pain, and thermal sensations to just below the nipples surmounted by a zone of decreased sensation over the nipples. The upper extremities showed no change. Incontinence of urine was present, but Guillain believes this was really due to an automatic bladder. Examination of the spinal fluid showed xanthochromia 8 cells, an albumin content of 1.70, increased globulin, negative Wassermann reaction and a colloidal benzoin reaction of 1112220000022210. Lipiodol injected into the cisterna magna showed an incomplete arrest extending from the lowest cervical to the sixth thoracic vertebra. Most of the lipiodol was in this region and appeared as linear bands, horizontal and vertical, and in granular forms of varying sizes. Roentgenographic interpretation of this picture was difficult since it did not correspond to the customary picture of tumor or pachymeningitis. In 1924, an operation performed in the area of the first five thoracic vertebrae revealed an abnormally blue dura mater. Under this was found a lacework of vessels, blue and tortuous, with the appearance of varices. This varicosity was on the posterior surface of the cord, which was completely covered with the vessels, and communicated with vessels in the substance of the cord. The condition of the patient remained the same after operation.

The clinical story of this patient is that of compression of the cord with a typical symptomatology, save for the character of the pains and their occurrence in crises. Operation showed the compression to be due to large varicosities on the posterior surface of the cord; the involvement of the anterior surface could not be ascertained. The nature of the pathologic process has been variously reported: (1) cirsoid aneurysms (Raymond and Cestan) when the process involved veins, arteries, and capillaries, causing a true myelitis, both sclerotic and cavernous, by penetration of the dilated vessels into the interior of the cord; (2) circumscribed varicose venous dilatations, as for example in the cases of Gerhardt, Lorenz and Sargent; (3) diffuse varicose dilatations, which are the most numerous, involving at least five or six segments; (4) Guillain and Alajouanine suggest the term angiocele of the spinal pia mater for the cases not falling into the other groups.

The clinical picture of these cases of cord compression is variable also. At times the course is so rapid as to suggest myelitis; more often it is slow in evolution. The majority of cases show spastic paraplegia due to compression. In the case of Raymond and Cestan the picture was unilateral. The spinal fluid is frequently xanthochromic. Lipiodol has been used in two cases by Sargent; in one it descended to the culdesac, and in the other there was an incomplete arrest. The evolution of the cases is usually slow, but sometimes it is interrupted by hemorrhage from the varicose veins. Sargent stresses the

variability in evolution of the process and the history of attacks with more or less complete remissions as indicating the vascular nature of the process. In the case of Spiller and Frazier there was a "remission" lasting eight years. As a rule, however, the cases are steadily and slowly progressive.

ALPERS, Philadelphia.

THE PROPER CLASSIFICATION OF THE CEREBRAL PALSIES OF EARLY LIFE. B. SACHS, Am. J. M. Sc. **171**:376-386 (March) 1926.

Sachs states that the palsies which occur early in life are evidently due in some cases to prenatal causes and in others to difficulties in labor, while in another group are the acute or acquired palsies. The presence of spasticity and the absence of changes in the electrical reactions, and the slight atrophy of the muscles, all help to differentiate between the cerebral and spinal palsies of early life. In a series of 225 cases, the author and Peterson noted that there were eighty-one right hemiplegias, seventy-five left hemiplegias, thirty-nine diplegias and thirty paraplegias; and of the total, 134 patients were males and ninety-one were females. On clinical grounds Sachs finds no objection to the establishment of a large number of types, but he feels that some confusion exists because of the fact that many authors have spoken of Little's disease as though it were a distinct clinical entity. Many practitioners speak of all congenital diplegias and paraplegias as Little's disease. Used in this way the name is an entire misnomer. If used, it should be restricted to forms of spastic paralysis, whether unilateral or bilateral, that can be definitely ascribed to difficulties during labor or premature birth.

In classifying the infantile cerebral palsies, the author divides them into three groups.

Classification of Infantile Cerebral Palsies

Group	Clinical Forms in Order of Frequency	Morbid Lesion
I. Paralysis of intra-uterine onset	Diplegia, paraplegia, hemiplegia	Large cerebral defects (porencephaly), defective development of pyramidal tracts; cortical agenesis (highest nerve elements involved); polioencephalitis (?); primary neuronal degeneration
II. Birth palsies	Diplegia, paraplegia, hemiplegia, di-ataxia, cerebellar form.	Meningeal hemorrhage, rarely intracerebral hemorrhage. Later conditions meningoencephalitis chronica; lobar sclerosis and cysts; partial atrophies
III. Acute (acquired) palsies	Hemiplegia, paraplegia, diplegia, choreic and athetoid disorders (unilateral and bilateral)	Hemorrhage (meningeal and rarely intracerebral); thrombosis (from syphilitic endarteritis and in marantic conditions); embolism. Later conditions: atrophy; cysts and sclerosis (diffuse and lobar); meningitis chronica; acute encephalitis (cortical and striatal); polio-encephalitis acuta (Strümpell)

In reviewing a few significant clinical facts, Sachs finds that the palsies due to intra-uterine disease and those due to traumatism during labor give a distinct history of early onset of all the symptoms. Bilateral palsies are more common

than in the acute cases, but the paralysis is not necessarily complete. He says that there can be no doubt that hemorrhage, embolism and thrombosis, the conditions which give rise to apoplexies in the adult, are important factors in the causation of the acute cerebral palsies in children. What appeared to be true apoplexies in the adult were observed in a recent epidemic of lethargic encephalitis, and the author concludes that both in the adult and the child, vascular lesions may be a frequent cause but not the sole cause, and in childhood he is convinced that an encephalitic process of any of the well known infectious types, lethargic, influenzal or what not, may be a cause of these acute cerebral conditions.

Sachs in conclusion cautions that it will not be safe to consider the globus pallidus or the putamen or the striatal system, as a whole, the sole site of the infantile cerebral palsies. The association of idiocy, imbecility, epilepsy and the more frequent occurrence of convulsions in the cerebral palsies of children compel the conviction that the cortex must not be overlooked. Very careful examination of the brain is needed to establish the complete pathologic record of these acute infantile palsies. It is most important to determine, whatever the form may be, whether the palsies are due to a morbid process that had its beginnings in the prenatal period or at the time of birth, or whether they were acquired later in life as the expression of vascular accident, or as the result of an infectious encephalitis.

TEMPLE FAY, Philadelphia.

CLINICAL MANIFESTATIONS AND PATHOLOGIC HISTOLOGY OF TABETIC PSYCHOSES. A. JAKOB, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:227, 1926.

"The question of tabetic psychoses is still unsettled both from the clinical and anatomic viewpoint." German investigators, like the French, emphasize the difficulties of establishing a clinically and anatomically sound tabetic psychosis, even though psychic disturbances occur in tabes not uncommonly, apart from undoubted general paralytic diseases. Such psychoses usually have a paranoid coloring mingled with auditory hallucinations and a slight loss of intellectual capacity. Cassirer and Meyer mention the frequent occurrence of paranoid psychoses, and Meyer found thirty cases with paranoid hallucinations in thirty-six psychoses not accompanied by general paralysis. Schultz has reported a case of tabes with involutional melancholia and one with dementia paranoides. All these authors, however, see no connection between the tabes and the psychosis and consider their occurrence together as entirely accidental. V. Rad reports the occurrence of outspoken psychic disturbances in twenty-five of 250 cases of tabes; of these, four were hallucinatory, ten showed severe character changes and three had short delirious conditions. Brodniwicz reports similar observations and believes that tabetic psychoses occur in two forms—a rapid and a slow form. Plaut groups the paranoid hallucinations occurring in tabes with those occurring without tabes and believes they were syphilogenous. Bumke is skeptical as to the occurrence of tabetic psychoses and groups the paranoid hallucinations occurring in tabes with the hallucinations of syphilitic patients.

Anatomic findings in such cases are very scarce. Sioli, in 1910, reported a case of tabetic psychosis which showed, besides the typical findings of tabes, a low grade meningitis over the brain, and degenerative changes in the cortex with specific changes in the vessels. Sioli grouped the case with those of

stationary general paralysis. Alzheimer found typical general paralytic changes in many cases of tabes with confusion which showed no evidences of general paralysis clinically. Schröder reported a case of tabes with paranoid hallucinations in which he found, in addition to the typical tabetic changes, a syphilitic meningo-encephalitis in the cord with Heubner's endarteritis in the larger pial vessels, and slight infiltration of the cerebral pia with lymphocytes and plasma cells. The pial vessels showed syphilitic changes. Schröder stated that a number of the tabetic psychoses have nothing at all to do with tabes, but are psychoses with spinal syphilis. There are cases of tabetic psychoses, however, he admits, that are in close etiologic connection with tabes. Urechia (1922) reported two cases, one of which showed marked pial infiltration in the brain, while the other showed vascular infiltration of a focal nature. Freund reported a case of tabes with syphilitic disease of the cerebral vessels. Finally, Jakob, in 1922, pointed out atypical findings in cases of tabetic psychoses in the form of focal disturbances.

Tabetic psychoses may be divided into the following groups: (1) Tabes with definite psychoses which clinically and anatomically are due to general paralysis. Many cases show a mild degree of general paralysis—mild meningeal and vascular infiltration, parenchymatous changes and iron reaction; the presence of red cells by Hortega's stain is characteristic. These cases can be grouped in Spielmeyer's group of abortive general paralysis. (2) Cases with definite vascular and parenchymatous changes of the nature of endarteritis syphilitica of the small vessels. (3) Cases with vascular changes not unlike ordinary arteriosclerosis. How much of a factor syphilis is in these cases is hard to say. (4) Cases with no characteristic findings but with definite changes. Such are the cases which Jakob reports.

Jakob reports several cases. The first is a case of tabes with short apoplectiform insults, confusion, intelligence defects and speech and motor disturbances. The serologic findings were strongly positive. The clinical diagnosis was tabetic type of general paralysis. Histologically, vascular changes were found which had nothing to do with general paralysis, and which were of the nature of endarteritis syphilitica of the small cerebral vessels. Relatively severe parenchymatous changes were found. A second case of a similar nature is reported but with less marked changes—vascular changes (endarteritis syphilitica) and slight parenchymatous changes. Still a third case of this sort is cited. Two cases of infiltration in the meninges are also reported.

Jakob raises the question as to whether the changes in the cortex have any connection with tabes, whether they are syphilitic in origin, and whether they represent a characteristic or pathognomonic finding. He believes that the changes found in his cases bear a similarity to the vascular and parenchymatous changes in endarteritis syphilitica, and are abortive cases of this process. He states that the brain pathology is syphilitic, a view strengthened by the fact that he was able to cite and briefly report two cases with similar findings, syphilitic in nature, but without tabes. Jakob says that the brain changes in tabetic psychoses are dependent on a syphilitic process and have therefore a common origin with the tabetic process. He believes, moreover, that he has been able to establish tabetic psychoses on an anatomic basis. Organic changes are present in these brains, but are not characteristic. There are diffuse parenchymatous changes of a slight nature and slight vascular changes. The changes are, therefore, not characteristic or pathognomonic.

ALPERS, Philadelphia.

THE MECHANISMS OF SPEECH AND DEGLUTITION IN PROGRESSIVE BULBAR PALSY. MACDONALD CRITCHLEY and CHARLES S. KUBIK, Brain **48**:492 (Dec.) 1925.

Except for the interesting reports by Dejerine and Collier, few references exist in the literature concerning the bulbar muscles in Charcot's disease. The authors analyze in detail the phenomena of normal articulate speech and deglutition, isolating the various component mechanisms and treating each separately; coughing, yawning, humming, laughing, crying, and sniffing are likewise discussed. The subject is also approached from a comparative morphologic and embryologic point of view, and then six clinicopathologic cases of amyotrophic lateral sclerosis are presented, with special emphasis as to bulbar involvement.

In all six cases there were severe cell changes in the nucleus ambiguus with little alteration in the dorsal vagal nucleus. The microscopic examination of the muscles subserving speech and deglutition in these six cases of progressive bulbar palsy demonstrated that no part of the musculature was exempt. There was severe atrophy of the intrinsic musculature of the tongue; the intrinsic muscles of the larynx showed definite and extensive atrophy; the elevator and depressor muscles of the larynx showed definite atrophic signs, but less severe than the intrinsic laryngeal musculature; the palatal muscles showed definite pathologic changes, while the constrictors of the pharynx were but little changed. The general pathologic condition in the muscles was a simple regressive atrophy of the muscle fibers characterized by an increase of the sarcolemma nuclei, longitudinal splitting of the muscle fiber, disappearance of the myoplasm and later of the sarcolemma and nuclei, with an increase of interstitial connective tissue between the bundles. In many cases in which there was a complete loss of function of various muscle groups on clinical examination, the atrophy later found histologically was patchy, many normal muscle fibers being present; this disparity between paralysis and atrophy may be explained by involvement of the upper as well as the lower motor neuron.

The morbid physiology of the progressive anarthria is explained by the authors as due to a steadily advancing affection of all the muscle elements of speech, comprising both the intrinsic and extrinsic laryngeal muscles and the muscles of lips, tongue and palate; the morbid physiology of dysphagia is explained by weakness of the lips and tongue and particularly by implication of the mylohyoid muscle, as this muscle by its contraction is the chief factor in propelling hard morsels and fluids through the pharynx.

The chief vocal effects of intrinsic laryngeal atrophy are: (1) the voice loses first its full compass and its power of registering falsetto notes; (2) the normal inflections and modulations of vocalization are lost and speech assumes a monotonous character; (3) the clear timbre of normal speech is marred by harsh and raucous overtones; complete aphonia, however, does not occur.

Paralysis of the extrinsic laryngeal muscles occasions difficulty in speech, in deglutition and in respiration. The speech affection comprises difficulty in singing high and low notes and inability to whisper. The subhyoid group of muscles also act as accessory muscles of respiration.

The effects of palatal implication in this disease are: (1) a nasal and blowing quality of the speech; (2) regurgitation of fluids through the nose, a rare phenomenon in this disease, owing to the low intrabuccal pressure; (3) inability to yawn; (4) inability to sniff, hum or blow the nose.

Involvement of the tongue leads to difficulty in conveying the bolus of food from the forepart of the mouth to the anterior pillars of the fauces, and is likewise responsible for much of the dysarthria, particularly in the pronuncia-

tion of linguals. The power of expectoration is lost early due to implication of the lips and tip of tongue, which is usually among the first of the bulbar manifestations.

STACK, Milwaukee.

ON THE CELL AND ALBUMIN CONTENT OF NORMAL CEREBROSPINAL FLUID AND THE SIGNIFICANCE OF SMALL INCREASES IN CELLS AND ALBUMIN. AXEL V. NEEL, Schweiz. Arch. f. Neurol. u. Psychiat. **17**:3-18, 1925.

As previously reported, Neel found that the cell count of normal spinal fluid was from 0.3 to 1.3 cells per cubic millimeter. Subsequently, he used a large Fuchs-Rosenthal chamber which held 7.2 cmm. instead of 3.2 cmm. About 5 cc. of fluid was removed for these examinations. He found that the cell count in the first 0.5 to 1 cc. was slightly higher than that of the last portion withdrawn. He is convinced that two or three successive cell counts exceeding 1.3 cells indicate a pathologic process. His procedure in examining spinal fluid is essentially as follows: One counting chamber is filled with a part of the fluid withdrawn first and another with part of the fluid obtained last. During the two or three minutes required to allow the cells to settle 0.1 cc. of Pandy's fluid is put into a test tube to which a drop of spinal fluid is added. Should a reaction take place, both globulin and albumin contents are determined. Should no immediate reaction take place, as viewed against a dark background in diffuse daylight, he regards the globulin content as so small that further examination is unnecessary. In order to obtain an approximate value of the quantity of albumin present he adds five drops of spinal fluid to the solution noting whether a reaction takes place with each additional drop. The Pandy reaction is predominantly a globulin reaction.

Neel found that a reaction produced by the addition of one drop of spinal fluid contains approximately globulin 1 and albumin 10, or globulin 0 (?), albumin 12 to 13; 2 drops, albumin 10; 3 drops, albumin 9; four drops, albumin 8; 5 drops, albumin 7 to 6. In order to obtain as precise a layering as possible in the nitric acid test, the pipet through which the acid (28 per cent) is introduced should be as pointed as possible. The reaction is read after three minutes. If the Pandy reaction is positive with the addition of one drop of spinal fluid, the globulin content must be determined. Spinal fluid 0.5 cc. is brought in contact with 0.5 cc. of a saturated solution of ammonium sulphate, neutral to litmus paper. Should this reagent be acid, proteins other than globulin enter into the reaction and too high a figure will be obtained. The reaction is noted after three minutes. Since these two solutions refract light differently, the reaction is checked by shaking the tube as it is done in performing the Guillain-Nonne-Apelt test. For the estimation of the total protein content, the material used in the original globulin reaction is employed. The precipitated globulin is dissolved by adding enough sodium chloride solution to give a dilution of 1-10. By further dilution the nitric acid figure may be obtained. Neel's conclusions are based on the examination of 2,448 cases, of which 425 were normal and 2,023 pathologic.

WOLTMAN, Rochester, Minn.

CLINICAL OBSERVATIONS ON CRANIOTABES AND RICKETS. S. J. WILSON and M. SELDOWITZ, Am. J. Dis. Child. **5**:603 (May) 1925.

The purpose of this study was to determine the relation of craniotabes to rickets, the incidence of craniotabes, the influence of age and season and the results of treatment. Careful differentiation was made between softening of

the bone suture lines and "true craniotabes," which, taken literally, means "wasting of the cranium." It is a condition in which there is softening of the bones of the skull, at times associated with rickets and also with congenital syphilis. It may also exist without either of these conditions. Two types are noted: the extensive soft skull giving a membranous sensation, and the thin, dry skull giving a crackling parchment-like sensation.

In a series of 469 babies under 1 year of age, 35 per cent had craniotabes and 25 per cent showed clinical rickets. Of those having rickets only 39 per cent had craniotabes; while of those having craniotabes only 29 per cent had or later developed clinical rickets; also in a small group chosen at random, 29 per cent showed rachitic changes in the long bones.

The authors assert that neither feeding nor sex influences the incidence of craniotabes, but that there is a greater predisposition in the colored than in the white child. The incidence of craniotabes is greatest between the third and fourth month of the first year, while that of rickets is greatest during the third and fourth quarter of the first year. There was a gradual increase in the number of cases during late spring and early summer and an almost complete absence of the disease in winter. The incidence of craniotabes was decreasing while that of rickets was still increasing.

One hundred and six of the babies in the series were divided into three groups. The first group was treated by cod liver oil in doses of from 0.5 to 1.0 drachm (2 to 3.5 cc.) three times a day. The second group was treated by exposure to direct sunlight for fifteen minutes twice daily. In the third group the mothers were instructed as to diet. In the first group only 33 per cent of the patients were well at the end of three months, while in the second group craniotabes had disappeared in 42 per cent at the end of the first month and in 91 per cent at the end of three months. In the third group, 61 per cent showed an absence of craniotabes at the end of three months. Thus, heliotherapy was found to be the best method of treatment, adjustment of the mother's diet was of considerable importance in breastfed infants, and the use of cod liver oil was of comparatively little value. It was also noted that in a large percentage of cases craniotabes disappeared during August and September, and that season was more important than age in the ultimate freedom from the condition.

WAGGONER, Philadelphia.

SOME OF THE POTENTIAL PUBLIC HEALTH HAZARDS FROM THE USE OF ETHYL GASOLINE. FREDERICK B. FLINN, J. Indust. Hyg. **8**:51 (Feb.) 1926.

In the experimental work goats and monkeys were employed in addition to the usual laboratory animals. The work included skin absorption and fume hazard tests, as well as tests calculated to show the effect of the natural evaporation of the ethyl gasoline. A few experiments to indicate the possible hazard from contact with tetra-ethyl lead were also carried out. Animals exposed to skin application of ethyl gasoline as well as those exposed to the fumes of dilute ethyl gasoline stored lead. The rate of excretion does not equal the rate of absorption. If, however, the animal, after a few nonlethal exposures, is given a free interval of several days, he will show marked improvement, though appearing somewhat sick. This may account for the fact that, so far, no cases of lead poisoning have been found at filling stations or in garages. The author agrees with Harnack who showed that triethyl lead acted as a whole molecule on the circulatory and respiratory centers for a short

period, and if the animal survived this period, the compound broke down, inorganic lead compound was formed in the body and all the secondary symptoms were those of inorganic lead poisoning.

During the experimental work, observations were noted in two persons who had closely followed the work, but had taken precautions to protect themselves, and yet stored lead. These persons complained of wakefulness at night, irrational dreams, nervousness and a general feeling of malaise. This is in keeping with the symptoms noted in the patient observed at the Reconstruction Hospital, New York, who died from tetra-ethyl lead poisoning. Persistent insomnia, marked restlessness and talkativeness with delusional states were noted. Exaggerated movements of all the muscles of the body were also present. Necropsy revealed no gross pathologic findings and without chemical examination or a knowledge of where the patient worked it was impossible to state that lead was the cause of death.

SCHUMACHER, Philadelphia.

THE METABOLISM OF OBESITY. THE DISTRIBUTION OF ENERGY PRODUCTION AFTER FOOD. CHI CHE WANG and SOLOMEN STROUSE, with the technical assistance of ALICE D. SAUNDERS, Arch. Int. Med. **36**:397 (Sept.) 1925.

This is the fourth of four articles on the metabolism of obesity, and is concerned with the distribution of energy derived from the various nutriments, by obese, normal and thin people following ingestion of meals high in protein, carbohydrate and fat, respectively. There is no demonstrable dependence of obesity on food intake or caloric balance. Nor is there any proved consistent relation between constitutional obesity and basal metabolism. Obese people show a lower specific dynamic action of protein following a high protein intake than normal or thin people. Obese people tend to derive their energy from carbohydrate when on a high protein diet, whereas normal and thin people use less carbohydrate than during starvation. Calories derived from fat decrease in the obese after the meal but show little change in thin and normal people. The two latter groups show a rise in calories from protein after the meal, but there is little change in the obese. More energy is derived from carbohydrate after a high carbohydrate meal and less from fat, while calories derived from protein vary little in any type of subject. All types show an increase in energy from fat after a high fat meal, but the obese continue to use carbohydrate in greater amounts than either normal or thin people. The protein consumption shows little change in this group. The explanation offered for excessive fat storage is that obese subjects derive less energy from fat, as indicated by the use of carbohydrate in greater amounts than either normal or thin persons after a high fat meal.

WAGGONER, Philadelphia

VASECTOMY AND ITS INFLUENCE UPON ONE HUNDRED CASES OF DEMENTIA PRAECOX STUDIED AT THE MANHATTAN STATE HOSPITAL. MAXIMILLIAN STERN, RALPH FOLSOM and I. SIDNEY RITTER, State Hosp. Quart. **10**:404 (May) 1925.

The author reviews the literature and shows that certain changes occur in the testes of patients with dementia praecox. These changes are a reduction and eventual disappearance of Leydig's cells, an increase of the interstitial connective tissue, atrophy of the seminal tubules and an arrest of spermato-

genesis. From the literature he then shows that vasectomy stimulates the endocrine activity of the testis and the patient is given a continuous dose of his own gonadal hormone, which in turn exerts a stimulating influence on the other glands of internal secretion.

Vasectomy was performed, in a prescribed manner, on 100 dementia praecox patients. The patients chosen for the operation were all under 30 years of age at the time of admission to the hospital and had been in the hospital from one to nine years. At the time the article was written, five months had elapsed since the last and eighteen months since the first operation was performed. The results at this time were: Eighty-eight showed no mental improvement; in seventy-seven there was no improvement physically; the degree of mental and physical improvement in the remaining twelve and twenty-three cases was so slight as to be negligible. No change in the testes or prostate was seen in 78 per cent. A few showed slight changes in the density and consistency of the testes. There was practically no change in the masturbatory tendencies: 4 per cent lost weight and 73 per cent showed no appreciable change.

HOWARD, Milwaukee.

VALUE OF NONSPECIFIC PROTEIN THERAPY IN SYPHILIS. SIGMUND S. GREENBAUM and CARROLL S. WRIGHT, Arch. Dermat. & Syph. **12**:858 (Dec.) 1925.

In secondary syphilis the lesions, as a rule, showed some involution after two or three injections of 4 per cent suspension of milk protein, and in a number of cases 75 per cent of the lesions had involuted after the sixth injection. Tertiary lesions responded even more favorably. To test the influence of nonspecific therapy as an adjunct to other and more powerful antisyphilitic remedies, twenty-five cases of latent syphilis, the patients presenting no evidence of syphilis other than a positive Wassermann reaction, were treated in this manner. For comparison, a second series of twenty-five patients with latent syphilis were treated by neo-arsphenamine alone. Only cases with a strongly positive or moderately positive Wassermann reaction were used, no attention being paid to the duration of the disease or to the amount of treatment previously given. Thirteen of the twenty-five cases treated with combined nonspecific and specific therapy, as against seven of the twenty-five cases treated with specific therapy alone, remained persistently negative (this study is less than a year old). It required an average of 4.7 injections of combined nonspecific and specific therapy, as against 7.5 injections with specific therapy alone, to obtain negative Wassermann reaction. Following Wenhardt, the authors suggest that the protein therapy serves to stimulate normal protective mechanisms within the body, and if this be true, nonspecific protein therapy should prove a valuable adjunct to the usual antisyphilitic remedies.

SCHUMACHER, Philadelphia.

SPINAL CORD TUMORS. REPORT OF SIX CASES. MAX H. WEINBERG, J. Nerv. & Ment. Dis. **63**:23 (Jan.) 1926.

The author reports six cases of spinal cord tumor, four of which as verified by operation were respectively glioma, hemangioma, endothelioma and tuberculoma — thus representing all the various tissues included under cord tumors. The study of these cases showed that differentiation between intramedullary and extramedullary tumors is difficult and at times impossible. The tendency

of the patient to stress his chief annoyances may render a history misleading by the overlooking of minor occurrences. The diagnosis of exact localization is difficult; it demands careful study and some training of the patient to distinguish extremes as well as degrees of sensibility. For this reason the first two examinations of sensibility are of little value. The roentgen ray is helpful in excluding bone lesions. Lipiodol injections in selected cases are useful for localizing lesions. While the sequence of symptoms is very important for their correct valuation it must be remembered that there is no constant or infallible symptom. The author cites a case of tumor pressing on the posterior columns causing very slight loss of deep joint sensibility. Operation is indicated in the majority of cases and laminectomy should be regarded as a justifiable and safe exploratory procedure in doubtful cases. Deep roentgen-ray therapy is especially important in inoperable tumors and is usually harmless although swelling of the neoplasm and decubitus have been reported.

HART, Philadelphia.

PRIAPISM FROM CORD LESION PRESUMABLY LUETIC. PARKE G. SMITH and CHARLES E. KIELY, Am. J. Syph. **8**:738 (Oct.) 1924.

The patient, a white man, aged 38, about six months before he was first seen, developed a state of priapism lasting thirty-six hours. Since then there had been some slight rigidity of the corpora cavernosa on both sides. Two months before he had another attack of priapism lasting three days. Four days before coming under observation the condition returned. The patient denied syphilitic infection, although admitting urethritis twelve years before. The pathologic findings were abolition of the knee jerks, the scar of a definite genital lesion, a slight general adenopathy, especially of the epitrochlears and an increased spinal fluid cell count (15 per cubic millimeter), lymphocytes predominating. Four days after the exhibition of 0.6 Gm. sulpharsphenamine together with large doses of iodides by mouth and intravenously, there was a marked improvement in the condition. On the sixth day the muscular spasm was entirely relaxed, although there was still some rigidity of the shaft. Sulpharsphenamine 0.6 Gm. was given on this date and again five days later when the patient reported a physiologic erection the night previous and its disappearance without trouble. The patient was seen again two months later and then showed the left pupil wider than the right and inactive to light. This symptom disappeared likewise under antisyphilitic medication. There seems justification, then, to ascribe the priapism to a syphilitic cord lesion.

SCHUMACHER, Philadelphia.

SO-CALLED ACRODYNIA OR ERYTHREDEMA (SWIFT'S DISEASE). A. S. WARTHIN, Arch. Path. & Lab. Med. **1**:64 (Jan.) 1926.

Two cases of erythredema, studied pathologically by Warthin, showed essentially the following changes: extreme edema of the meninges and brain, with dilatation of the central canal of the spinal cord. There was proliferation of the meningeal and perivascular reticulo-endothelium, both in the nervous system and around a few of the peripheral nerve trunks. No degenerative or inflammatory changes were found either in the central nervous system or in the nerves. There was chronic erythema of the skin, with hyper-

keratosis, hypertrophy of the epidermis and sweat glands, slight pigmentation of the rete and hypoplastic lymphatic constitution. There was associated or terminal respiratory infection, gastro-intestinal catarrh and inanition.

The changes in the skin and nervous system suggested the pathologic changes of the early erythema stage of pellagra, and the skin changes were identical with those occurring in light sensitization and in certain stages of roentgen-ray and ultraviolet-ray erythemas. Warthin considers that the entire anatomic picture resembles that due to a food deficiency or a toxic state in persons of the hypoplastic constitution, affecting the reticulo-endothelial system of the meninges and skin, and the vegetative nervous system, and possibly leading to light sensitization.

PEARSON, Philadelphia.

PROTEIN SENSITIZATION IN EPILEPSY—A PRELIMINARY REPORT. J. FRANCES WARD and HAROLD A. PATTERSON, State Hosp. Quart. **10**:429 (May) 1925.

After a comprehensive review of the literature on protein sensitization the authors conclude that a local inflammatory reaction may occur in the meninges of sensitized persons as well as anywhere else. Such a reaction could cause a swelling that would exert pressure on the sensory and motor centers and thus produce the well known symptoms of epilepsy. In this preliminary report, 100 epileptic patients were tested with group allergens. In 50 per cent of all cases tested there was a positive reaction; the preponderance of patients reacted to the fish group, the next greatest number to fowl and the third to vegetables. With the individual proteins about 50 per cent again showed a positive reaction. In this test the oat protein predominated, and lactalbumin was second and cauliflower third.

No therapeutic measures have yet been instituted, but the authors anticipate that a great deal can be accomplished toward reducing epileptiform seizures by determining the protein responsible for the irritation of the meninges.

HOWARD, Milwaukee.

MENTAL HYGIENE IN INDUSTRY. HENRY B. ELKIND, J. Indust. Hyg. **6**:113 (July) 1924.

The adjustment of the employee to his industrial environment is the aim of both the mental hygienist and the personnel worker. The results of a group psychologic test given to a group of employees of a mercantile establishment showed that there is some positive association between native intelligence and clerical ability. As a result of the study it has been found that there is great need for the utilization of mental hygiene in the employment department, not only in the acceptance and placement of the applicant but also in the matter of adjustment to environment or situation. Mention is made of the incidence of functional nervous disease among the employees of a large department store and of a large public utility office. The case incidence of functional nervous disease in the former was about 10 per cent and it stood fourth in the order of frequency of complaints treated in the store health dispensary. The case incidence in the public utility office was about 6 per cent; it was fourth in number of cases and fifth in rates.

SCHUMACHER, Philadelphia.

THE FUNCTIONS OF THE REGION OF THE INFUNDIBULUM AND THE TUBER CINEREUM AND THEIR RELATIONS TO THE HYPOPHYSIS. GUSTAVE ROUSSY, Ann. de méd. **18**:407, 1925.

Many physiologic functions which were attributed to the internal secretion of the hypophysis are now considered as being dependent on centers surrounding the third ventricle. In his experiments on 149 dogs and forty-six cats Roussy has checked up earlier publications and has found new facts, which support the following conception of the rôle of the vegetative centers of the region of the tuber cinereum: The paraventricular nuclei contain a center for the regulation of the water metabolism; their artificial lesion produces polyuria and transient glycosuria. Other tuber nuclei regulate the fat metabolism; their lesion is followed by Froehlich's syndromes which could not be produced merely by removing the hypophysis without a lesion of the tuber cinereum. The only function now attributed to the hypophysis (its anterior lobe) is the regulation of the growth of the skeleton, which could not be influenced by artificial lesions of the tuber region.

WEIL, New York.

MORPHINE HUNGER AND THE SMOOTH MUSCLE REACTION: A STUDY OF THE HABITUÉ. S. D. LUDLUM and ELLICE MCDONALD, J. A. M. A. **86**:835 (March 20) 1926.

A study of the smooth muscle reaction as manifested by roentgenograms of the stomach and large intestine using a twenty-hour study of the vegetative innervation of the colon with immediate fluoroscopic observation of the barium meal in the stomach following administration of morphine in habitués in the absence of other drugs and purgatives is reported. Other drugs, endocrine extracts and salts were also studied. The authors conclude that morphine hunger is a state of increased sympathetic tonus and that morphine increases vagus preponderance of the vegetative nervous system as do magnesium and calcium salts. The hope in treating the habitué, therefore, manifestly is the correction of this physiologic unbalance by means of such substances as will reproduce vagus preponderance or correction of the sympathetic preponderance without producing the anesthetic or analgesic effects of morphine.

CHAMBERS, Syracuse, N. Y.

EXPERIMENTAL STUDIES ON DIABETES INSIPIDUS INFUNDIBULARE AND DIABETES MELLITUS OF THE TUBER. J. J. GOURNAY and ANDRÉ LE GRAND, Ann. de méd. **18**:434, 1925.

Leschke expressed the opinion (1919) that the polyuria following a lesion of the third ventricle is due to direct nervous stimulation of the kidneys. The authors, however, could not support this theory, finding that a lesion of the paraventricular region was followed by polyuria even after complete decapsulation and denervation of both kidneys in twenty experiments. The increase in water output was accompanied by an increase in purin bases in the urine; injections of hypoxanthin produced marked polyuria. Glycosuria could not be elicited so easily; only a localized lesion of the paraventricular nuclei in rabbits, not in dogs, was followed by glycosuria, which only lasted a few days. (Judging from the illustrations polyuria was produced by a lesion of the mesial tuber nuclei, glycosuria by a lesion of the perifornical nuclei of Spiegel and Zweig.)

WEIL, New York.

REPORT OF A CASE OF CEREBROSPINAL SYPHILIS TREATED BY INOCULATION WITH MALARIA PARASITES. E. C. THRASH, Am. J. Syph. **10**:94 (Jan.) 1926.

The author reports a case of cerebrospinal syphilis, first seen in 1922, intensively treated with arsphenamine, mercury, iodides and bismuth, and four intraspinal injections of mercurialized serum, which were given in 1924. No beneficial effects were observed as a result of this treatment; the patient steadily declined, physically and mentally, and in May, 1925, was uncontrollably demented. On June 30, 1925, tertian malaria was inoculated and resulted in a chill three days later. Chills occurred daily, with high febrile reactions, until July 15, when quinine treatment was started. Improvement was rapid, and in October the patient was permitted to return home, with no evidence of general paralysis, feeling well and having gained 28 pounds (13 Kg.). No conclusions are drawn regarding the permanency of the improvement.

KUBITSCHECK, Philadelphia.

TRANSPLANTATION OF THE GRACILIS MUSCLE FOR INCONTINENCE OF URINE. CLYDE LEROY DEMING, J. A. M. A. **86**:822 (March 20) 1926.

After a brief review of the literature on muscle transplants for epispadias and hypospadias, and of the incontinence consequent thereto, the author reports the case of a Jewish woman, aged 21, who originally had an epispadias and who had had several attempts made to control urination with no result, but with an excellent cosmetic result on the genitalia. He describes briefly his technic and points out that the use of the gracilis muscle is advantageous because it does not interfere with the locomotion of the patient; it is accessible and easy to transplant, and has a double nerve supply.

CHAMBERS, Syracuse, N. Y.

THE COLLOIDAL BENZOIN REACTION IN ACUTE POLIOMYELITIS. JOSEPH C. REGAN, Am. J. Dis. Child. **30**:844 (Dec.) 1925.

Using the colloidal solution of benzoin introduced by Guillain, Laroche and Lechelle (*Rev. neurol.*, January, 1921), Regan studied the effect of its reaction on the cerebrospinal fluid in twenty-three cases of acute poliomyelitis. Precipitation occurred in the meningitic zone. As the cerebrospinal fluid in epidemic encephalitis produces no reaction, the author suggests that the test provides an additional means of differentiating between the two diseases.

VONDERAHE, Cincinnati.

ON ENDOGENOUS AND EXOGENOUS FACTORS IN CHARACTER FORMATION. GEORGE A. AUDEN, J. Ment. Sc. **72**:1 (Jan.) 1926.

A twenty-four page discussion of the different conceptions that have been advanced of the relationships between bodily conformation and mental traits is presented. In a diagram the author illustrates his own schema of a fourfold basis of character with two biologic inheritable factors, which he calls somatic constitution and the innate quality of the brain on which intelligence depends, and two exogenous factors which he calls the social and individualistic trends.

BOND, Philadelphia.

Society Transactions

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, March 2, 1926

I. Abrahamson, M.D., *President, in the Chair*

SYMPOSIUM FROM THE NEUROLOGICAL SERVICE OF MOUNT SINAI HOSPITAL

A Case of Toxemia Presenting Unusual Clinical Manifestations, with Recovery. Dr. E. E. Arnheim (by invitation).

A woman, dressmaker, was admitted to Mount Sinai Hospital, Dec. 13, 1925, with a history of headaches for four months, vomiting for four weeks, and edema of the face for one week. On examination she was found to have edema of the face, "urinous" breath, anemia, enlarged heart, a mass in the right para-umbilical region, hypertension, and urine of low specific gravity, albuminuria and casts. Immediately after admission she began to have severe generalized convulsions. A diagnosis of uremia was made, but the blood chemistry figures were normal.

She was transferred to the neurologic service, December 29, because at various times she presented abnormal neurologic findings: papilledema, signs of meningeal irritation, transient amaurosis, and at one time definite focal signs, such as hyperactive deep reflexes on the right with absent abdominals, Babinski sign, and central right facial weakness.

The patient was discharged from the hospital January 23. During her stay there was a gradual clearing up of practically all abnormal findings: convulsions; albuminuria; microscopic picture of the urine; high blood pressure; jaundice, and papilledema. On discharge, the only abnormal findings were: unequal pupils, left larger than right; a slight nystagmus in horizontal planes, and a slight secondary anemia. At present, March, 1926, even these abnormal findings have disappeared. Blood and spinal fluid Wassermann reactions have been negative.

The case is remarkable because about every other day a new diagnosis was entertained, and because of the complete recovery. The only condition that could explain the multiplicity of findings in this case is a toxemia of some kind with toxic effects — cerebral, renal, vascular and hepatic. An infectious element is likely because a severe angina started the more serious illness four weeks ago, and a review of the temperature chart showed that the patient always had slight fever with coincident leukocytosis, her temperature dropping when the condition improved.

Arsenic was found several times in samples of the patient's urine in fairly large amounts. Clinically, however, the case did not resemble arsenic poisoning, and the source of arsenic, after long search, has not been revealed. However, the case is considered to be one of chronic arsenic poisoning for four months, with an infectious process superimposed.

SUBARACHNOID HEMORRHAGE. DRS. M. GROSSMAN and D. ARBUSE (by invitation).

Five cases in the neurologic service of Mount Sinai Hospital form the basis of the paper. In all the patients there was an abrupt onset with severe headaches, accompanied by nausea and persistent vomiting, and with pain and stiffness of the neck. The majority showed clouding of consciousness which varied from irritability to coma. The signs of focal disease of the brain were slight, but all showed evidence of meningeal involvement and a blood-stained cerebrospinal fluid. Three patients had fever on admission, and the other two subsequently. The blood and spinal fluid Wassermann reactions were negative in all.

CASE 1.—A housewife, aged 48, was admitted with the history that she suddenly began to suffer from severe headache eight days previously. The next day, pain, stiffness of the neck and vomiting began. The vomiting lasted for two days; the pain, stiffness and headache became progressively worse. The day before admission she began to have chills and some fever. She was acutely ill; the temperature was 100.5 F.; the urine showed a trace of albumin; the blood pressure was 140 systolic and 80 diastolic. The following conditions were noted: tenderness to percussion over the entire skull; both pupils dilated, the right reacting more promptly to light than the left; some hyperemia and blurring of the margin of the right disk; slight ptosis of the left eyelid; slight weakness of both external recti; facial asymmetry with deviation of the tongue to the right; deep reflexes of upper extremities diminished, knee and ankle jerks absent; abdominal reflexes present; no Babinski sign. There was marked rigidity of the neck and a bilateral Kernig sign. Lumbar puncture yielded a uniformly bloody spinal fluid under moderate pressure; a second lumbar puncture two days later showed a similar fluid. The patient was discharged, apparently well, twenty days after the onset of the illness. Ten months later she was still well, but later she died through an accident, the nature of which could not be ascertained.

CASE 2.—A truck driver, aged 32, entered the hospital complaining of severe headache and vomiting of nine days' duration. His illness began abruptly while he was lifting a heavy weight; he became weak, and "things suddenly became dark before his eyes." He was unable to continue his work and started for home; on the way he vomited and began to have severe headache. He went to bed and on account of severe nausea induced vomiting. He remained in bed two days, and then felt well enough to return to work. He was nauseated but stayed at his work the next day; on arriving home he again induced vomiting without relief. His family physician found a rigid neck, bilateral Kernig sign, and a positive right Babinski sign. Lumbar puncture showed a bloody spinal fluid. Five days before admission he had some difficulty in micturition.

On admission he was acutely ill and very restless, and complained of severe headache. His temperature was 102.4 F.; the urine showed a trace of albumin; the white blood count showed 17,000 cells with 73 per cent polymorphonuclear leukocytes. There was inequality and irregularity of the pupils, but they reacted to light and on convergence; nystagmus was present in both planes; there was a right facial weakness of the central type; the deep reflexes of both arms were diminished; the knee and ankle jerks were absent; there was a marked neck rigidity and a bilateral Kernig sign. Lumbar puncture showed a blood-stained spinal fluid.

The man was discharged, recovered, twenty-two days after the onset of the illness. Three days later, while on his way to a resort in New Jersey, he had a seizure on the ferry boat and died before the boat reached the Jersey shore. No necropsy was done.

CASE 3.—A tailor, aged 48, well up to four days before admission, suddenly became dizzy and had a severe headache. After taking some "bromo-seltzer" he promptly vomited. His headache persisted and he began to have diplopia and perspired freely.

Physical examination showed the patient to be acutely ill, very restless and complaining bitterly of severe headache. The white blood count was 14,500, with 73 per cent polymorphonuclear cells. There was percussion tenderness over the entire skull; both disks were blurred, the veins were engorged, but there was no measurable elevation; the left pupil was larger than the right, both were irregular but reacted promptly to light and on convergence; there was weakness of both external recti muscles, and slight right facial weakness of the central type; the right deep reflexes were more active than the left, and the right abdominal reflexes were diminished; the plantar responses were equivocal; there was a marked neck rigidity and bilateral Kernig sign. Lumbar puncture yielded 30 cc. of bloody spinal fluid under increased pressure. Later, there developed a frank papilledema with hemorrhages, which ultimately cleared up. Repeated lumbar punctures up to three weeks showed evidences of bleeding into the subarachnoid space.

CASE 4.—A housekeeper, aged 50, was admitted to the hospital with the history of a sudden attack of unconsciousness the day before, followed by severe headache, persistent vomiting and semistupor. Her left eye was "injured" forty years before, following which she had "weak eyes." She was also said to have had occasional headache for the last six months. On admission she was acutely ill and extremely restless, and vomited persistently. The tongue was dry and coated, and the breath foul. The temperature and blood pressure were normal; but the urine showed albumin and a few hyaline and granular casts. She had a widely dilated, fixed left pupil and a sluggish contracted right pupil. The question of the old trauma to the left eye had to be considered as a possible cause of the immobility of the left pupil; both disks showed mild arteriosclerotic changes; the eye movements were slightly restricted in both lateral planes; the deep reflexes were barely elicited in both the upper and the lower extremities; the abdominal reflexes were absent; the plantar responses were equivocal on both sides; the neck showed marked rigidity; lumbar puncture yielded a uniformly bloody fluid under increased pressure. She developed fever during the second week of illness, and a moderate left ptosis. Repeated lumbar punctures all showed evidence of the subarachnoid hemorrhage.

CASE 5.—A tailor, Polish, aged 41, complained on admission of severe occipital headache and vomiting of three days' duration. Four and a half years previously he had a sudden loss of consciousness following which he remained in bed for two weeks. His present illness began three days before admission with severe headache, vomiting which was profuse and not related to taking food, vertigo, stiffness of the neck, dulled mentality, trembling of the hands and general weakness. Examination showed the patient to be acutely ill, semistuporous, noncooperative. His temperature was 100 F. and pulse rate 60. Neurologically he showed unequal pupils; both, however, reacted to light and

in accommodation; his fundi were normal; there was slight weakness of both external recti muscles; he showed a slight right facial weakness of the central type; the deep reflexes were slightly more active on the right side; there was marked rigidity of the neck with a bilateral Kernig sign. Lumbar puncture yielded 18 cc. of bloody spinal fluid under moderately increased pressure.

Two days after admission he had a generalized convulsion, which was described as a tonic fit in which the patient's extremities assumed a decerebrate posture. Later that day he had another, and the next day he had two more similar seizures. Following these seizures he showed marked disturbance in his cerebellar functions. Vestibular tests, according to the otologist, pointed to an intracerebellar lesion. Six weeks after the onset of the illness, red blood cells were still present in his spinal fluid.

The clinical course showed steady improvement until the patient was discharged from the hospital about two months after the onset of the illness. Two months later, he reentered the hospital complaining of headache, vertigo, staggering gait, and weakness of both legs. Examination at this time showed inequality of pupils, papilledema, left homonomous hemianopia, astereognosis and disturbance of postural sensibility on the left side, and mild pyramidal tract signs on the left side. With these findings the diagnosis of a cerebral neoplasm was made. The spinal fluid at this time was clear, and showed 24 cells. He died about two weeks after the second admission and a cerebral neoplasm was found in the occipitotemporal lobe with considerable softening on the inferior surface.

On the basis of a number of parallel cases quoted from the literature which on necropsy showed rupture of an intracranial aneurysm, the readers of the paper felt that they could best explain the clinical syndrome presented by the first four of their five cases on the assumption that they were dealing with a hemorrhage into the subarachnoid space from a ruptured intracranial aneurysm.

DISCUSSION

Dr. D. Arbuse (by invitation): I have examined three of the cases reported, and curiously enough, one of the patients reported as completely cured I learned only yesterday had died. I tried to find out how the patient met death, but the family had moved, and a neighbor told me she had heard death was due to an accident.

I saw the woman, G. S., aged 49, on Dec. 5, 1925; at that time she merely complained of occipital headache, and told me she had lost 15 pounds in weight. Physical examination gave practically negative results. The fundi were normal; there were no signs of meningeal irritation. She had complained of persistent stiffness of the neck while in the hospital. Sensory examination was negative. All deep reflexes were present, but not active. When she came into the hospital, all deep reflexes were absent.

The other woman reported at present complains of headache in the left frontal region and dizziness. The positive neurologic findings are: ptosis of the left eyelid, and inequality of the pupils, the left being larger than the right. The left pupil is fixed to light. The fundi are negative except for moderate angiosclerosis. She has no signs of meningeal irritation and no loss of motor power. She has no pathologic reflexes; her mental status is good.

The man, A. S., shows practically no signs; all reflexes are present; the fundi are normal.

Dr. E. D. Friedman: The reference made by Dr. Grossman to the paper by Symonds is very timely. He has stressed this association of subarachnoid bleeding with the picture of acute meningitis. He has made it possible to diagnose many of these cases intra vitam. In one of the cases presented by Dr. Grossman, there was present a sign which Symonds described as giving additional evidence of subarachnoid bleeding, namely, hemorrhage in the fundus. While the ophthalmologist attributed these to another cause, we felt that they constituted further evidence of bleeding into the subarachnoid space, with extension of the hemorrhage into the sheath of the optic nerve. I am told by an ophthalmologist that this is possible. One must agree with Dr. Grossman that the cases presented, except the last which proved to be neoplastic, belong in this group of subarachnoid hemorrhage.

Dr. Simon Rothenberg: We see these cases when it is difficult to differentiate them from encephalitis or brain tumor. We have now a case at the hospital that has given great difficulty in diagnosis, in which hemorrhagic spinal fluid, without eye symptoms or papilledema, is present. The man presents a multiplicity of symptoms, which makes it difficult to localize the lesion. Whether it is an encephalitis is still a question. The point we have stressed as in favor of encephalitis has been the acute onset with multiplicity of symptoms and the blood in the spinal fluid. Yet, this case is difficult to diagnose as such because it is just as likely to be a hemorrhagic condition associated with aneurysm as an encephalitis.

Dr. I. Strauss: For the purposes of the record it would be well to correct Dr. Friedman's explanation of subarachnoid hemorrhage going through the optic sheath.

Dr. Friedman: I have already mentioned a case in a previous discussion of the subject before this society, when Dr. Sands presented a paper several months ago; but I should like to make reference again to this case in which I was able to make a correct clinical diagnosis. A patient was admitted to the hospital in stupor. There were evidences of subarachnoid bleeding, fever, meningeal phenomena and, at the same time, widespread hemorrhages in both fundi. Because of the coincidence of the meningitis syndrome, subarachnoid bleeding and the retinal hemorrhages, we believed that we were dealing with a perforating cerebral aneurysm. The postmortem examination revealed a rupture of the posterior communicating artery.

Dr. Grossman: I was able to find only two references substantiated by postmortem examinations; one was the case reported by Symonds who showed that the hemorrhage had passed forward in the sheath of the optic nerves, which were much distended with blood clot which ultimately tore its way forward underneath the retina. The second was a case comparable to the one cited above and it was reported by Bramwell.

Metastatic (Secondary) Brain Tumor. Drs. J. H. Globus and H. Salinsky (by invitation).

A survey of the clinical records and of the postmortem findings in a group of fourteen cases of metastatic (secondary) tumor of the brain was presented. It was pointed out that only in a few instances was the neoplastic character of the disease process recognized during life and still less frequently was the metastatic nature of the lesion suspected. It was suggested that one of the main diagnostic difficulties was found in the fact that in a large number of instances the primary malignant focus could not be detected and often was not even suspected. The conclusions drawn from the study of the fourteen cases were as follows:

Metastatic brain tumors are clinically characterized by: (1) an acute and often precipitate onset of cerebral manifestations, which are most commonly disjointed or disseminated in character, simulating a meningo-encephalitic process; (2) the symptoms of increased intracranial pressure, such as headache, nausea, vomiting and dizziness, are usually out of proportion to the rather mild objective neurologic findings; (3) papilledema is not common and occurs only when a tumor mass is present in a situation where it can obstruct the escape of cerebrospinal fluid from the lateral ventricles. (4) meningeal signs are not infrequent and pleocytosis is occasionally found as the result of direct invasion by tumor tissue of the subarachnoid space or subependymal structures; (5) a psychosis in this series of cases was a terminal event and cannot be regarded as a diagnostic feature.

DISCUSSION

DR. G. H. HYSLOP: In 1924, in *L'Encéphale*, fourteen cases of metastatic brain neoplasms were reported, and the clinical and pathologic observations were quite similar to those this evening. I have seen approximately a dozen similar cases at the Memorial Hospital, in which malignancy was proved. I mention these because of the fact that the readers of this evening's paper stress that the period between the diagnosis of malignancy following primary operation and the onset of intracranial symptoms leads one away from the belief that a malignant tumor in the brain may be present. The longest interval I recall was fifteen years in a woman with a breast carcinoma, and the clinical course of the intracranial metastases was characteristic, as has been brought out tonight. One thing might be added, and that is the frequency with which is found one large metastasis producing the focal major clinical symptomatology. The brain at necropsy may be riddled with metastases, and the numerous metastases perhaps account for the intracranial pressure symptoms without much in the way of signs. A French author found quite frequently a marked ependymitis with a certain amount of degeneration of the myelin tissue in the region of the metastases, which he held to be responsible for a meningeal reaction; this would explain the headache, vomiting and lymphocytosis.

DR. I. ABRAHAMSON: This is an important subject and is worthy of much discussion. It is interesting that these cases have shown a multiplicity of signs, but seem to have had only one large neoplasm. I personally feel that the brain must be riddled in these cases with minute foci of disease, because the clinical syndromes in most cases cannot be explained by a single tumor, and yet a single large tumor has been found. In one case mentioned by Dr. Globus, which six years later he reinvestigated, the patient presented a multiplicity of signs and symptoms, for at the time there was a discussion as to whether we were dealing with neoplasms or with an encephalitis. She had a pigmented mole on the leg which had been irritated by a garter. It became infected, and had to be removed. A year or two later a gland was removed from the groin, and the pathologic diagnosis at the time was melanocarcinoma. At that time I sought to explain this gland as possibly a lymphadenitis with melanin deposit in it from the infected mole below, and that the brain process was not due to a malignant tumor; but that this tumor was really a lymphadenitis loaded with melanin which had been deposited there from the infected pigmented mole. At the time I reasoned by analogy that if you transplant a negro skin on a white man, within a short time all the melanin is within the neighboring lymphatic glands. The skin becomes white, and we know that the melanin from an infected gland is carried to the nearest

lymphatic, and that was my explanation of the tumor then. I do not believe that this one large mass explained all the signs and symptoms that the patient presented. That is characteristic of these tumors. Metastatic tumors affecting the spinal column are multiple. They may present in the early days symptoms possibly in the cervical distribution, radiating pains, evidence of radiculitis, etc., and we suspect with a history of malignancy before that we are dealing with a malignant tumor. The symptoms may disappear from the cervical region and finally settle in another site and remain persistent; then a mass appears indicative of extensive destruction of the body of the vertebra. The roentgenogram in these cases is apt to be negative in 50 per cent of the cases until extensive destruction of bone has taken place, so at necropsy one frequently finds the entire column riddled with malignant tumors. This has been explained at the Montefiore Hospital by the fact that a secondary inflammatory process takes place about the neoplasm and localizes it and limits its spread. I think that the very rapid onset and the stormy course is a syndrome we ought always to keep in mind, because it will be of great assistance in diagnosing these conditions and guiding our efforts at therapy.

Dr. Louis Aronson: The presence of brain neoplasm with a fairly positive diagnosis is often associated with quiescent signs of neoplasm elsewhere for quite a long time, unsuspected, and then suddenly there is a blooming-out of many clinical signs of general carcinomatosis.

A woman, aged 38, on her way home from the mountains last September was suddenly taken with an attack of right-sided hemiplegia. She was irrational and aphasic, and was taken to the nearest local hospital. In the absence of syphilis and cardiac disease, the diagnosis most probable was that of a vascular condition. Months later she showed very mild haziness of the disks. A cerebral neoplasm was suspected and diagnosed. Nothing was found elsewhere. Gradually she lost weight and came down from 180 to 100 pounds (82 to 45 Kg.). I saw her about four days ago, and she now presents at least three masses in the abdomen, one under the liver, one enormous mass in the left side and one posteriorly connected with the ribs on the left side.

I mention this case because of the clinical rarity of intracranial symptoms, followed by a period of quiescence, and then the appearance of a general carcinomatosis in the abdomen, the intracranial symptoms having made but little progress.

Dr. Globus: I wish to stress one more point, and that is that roentgen-ray examinations of the skull yield no important information for the reason that a tumor with metastases to the brain will seldom metastasize into the bony tissues. On the other hand, tumors which frequently metastasize into the bony tissue do not metastasize into the brain. That is a very frequent occurrence in our necropsy material. We find frequently a metastatic tumor in the scalp or calvarium, but the brain is free of tumor invasion. In the fourteen cases presented, in no instance was there a metastatic nodule in the bony structure.

Pathologic Material. Three Cases of Primary Brain Neoplasm. Drs. I. Strauss and J. H. Globus.

The first patient, a woman, aged 33, four months before entering the hospital had given birth to a child. She became pregnant because she had been told that pregnancy would relieve her of deafness. She died, leaving another child in the world to care for. Her history dates back only two years. In these two years she had diminution of hearing in the left ear, and there was also

some staggering in gait. This was thought to be due to diminution of vision, and that she accommodated her gait more or less to the defect in vision which developed. The zigzag staggering gait came on very gradually. She had a tendency to fall to one side more than to the other. She complained of pain in the region of the right trigeminal nerve, and her only reason for entering the hospital was to be relieved of the pain in that region. The pain was typical of trigeminal neuralgia, very acute, and she suffered much from it. She had no convulsions, and no ataxia of the extremities. She had not suffered from headache or vomiting.

Physical examination at the time of admission showed she was deaf in both ears; that vision was markedly reduced by a concentric limitation of the fields. The fundi showed postneuritic atrophy, with some congestion of the vessels and a little blurring. She had a little facial asymmetry; a marked diminution of sensibility in the region of the left trigeminal nerve, and a possible slight weakness in one side of the body. It was remarkable that there was such a paucity of physical signs. She continued under observation without much change. Examination by otologists showed that the vestibular apparatus of both ears was affected. The conduction was lost. An examination by roentgen ray showed decidedly increased intracranial pressure. In order to be positive that we were dealing with a lesion of the posterior fossa (she had no cerebellar symptoms outside of the change in gait), we did a ventricular puncture, and that bore out the diagnosis of posterior fossa lesion, because it showed a definite internal hydrocephalus. She was operated on, stood the first stage well and died on the table suddenly while the second stage was being performed.

This woman had two tumors in the posterior fossa, one of tremendous size with marked deformation of the pons. It is interesting to see in the literature that occasionally there has been bilateral deafness with a tumor on one side. It is also interesting that Cushing had a case in which, likewise, there were so few symptoms pointing to internal hydrocephalus that the physician wrote him that he could not understand how this patient could have a bilateral tumor with so few symptoms. The case presented tonight is of that sort. A diagnosis of tumor in one angle was made. We were not certain, but some of us suspected the presence of a tumor in the other angle. One symptom showed that we were dealing with a large tumor: the vertical nystagmus, and toward the end of the illness, the loss of associated vertical movement of the eye. These two symptoms point to involvement of the brain stem. When the specimen is seen, it is surprising to think that this woman could have gone on for two years (probably the tumors existed before then) without any history of tinnitus, headache, vomiting or cranial nerve symptoms (except in the last few months when the irritative symptoms of the trigeminal region were present), and yet there could be such distortion of the pons by a tumor of enormous size.

Dr. Globus demonstrated the pathologic material and slides; the history of the second case was given by Dr. Grossman in the first presentation of the evening.

DISCUSSION

DR. GLOBUS: Metastatic carcinomas of the brain frequently present a clinical picture which is difficult to differentiate from one presented by spongioblastomas, the primary malignant tumors of the brain. This is likely due to the character of spongioblastomas, a form of brain tumor which may simulate almost any form of cerebral lesion, including metastatic brain tumor.

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, March 12, 1926

EDWARD A. STRECKER, M.D., *President, in the Chair*

VISUAL HALLUCINATIONS IN ORGANIC DISEASES OF THE BRAIN. DR. TEMPLE FAY.

The paper takes up the analysis of reported cases in the literature as to the localization of the lesions and the theories of the production of hallucinations from these lesions. The author adds eight cases to those already reported, four of them verified by necropsy and one by operation. In summarizing the present view as to the location of lesions capable of causing visual hallucinations, three claims have been made. In one group of writers the occipital lobe has been reported and emphasized as the probable site of the lesion giving rise to hallucinations of this type. In the second group are those who believe the temporo-occipital lobe is the probable area involved in their production, whereas it has been pointed out by a third group that hallucinations occur in other portions of the visual pathways, even distant to the cortical areas, so that it seemed necessary to weigh the evidence at hand to determine what factors were common in all three groups. The discussion following Horrax' excellent paper in 1923 showed an agreement on the fact that crude hallucinations of light and color were frequently to be associated with occipital pole involvement, whereas formed hallucinations occurred when the lesion was placed more anteriorly in the temporal or temporo-occipital lobe.

The author found in an analysis of the cases reported that occipital lobe tumors, in giving rise to hallucinations, involved not only the cortex, but also the optic radiations. The verified case of temporal lobe tumor likewise involved the radiations and the optic thalamus. Many cases were found in the literature in which the lesion was in the region of the optic tracts or nerves outside of any cortical areas which could give rise to memory cell irritations. In the eight cases reported in the author's series, with four verified by necropsy, two were interpeduncular tumors, adamantenomas involving the optic tracts behind the chiasm, one was a primary pituitary tumor, one an endothelioma of the left cerebellopontile angle, and one a case of occipital pole tumor verified at operation. Two cases were probably temporal lobe tumors, though unverified, and one was an unverified pituitary tumor.

In view of the similarity of optic pathway involvement in all three groups, and from the analysis of the four verified extracerebral cases in the author's series, it seemed evident that cortical irritation or memory cell involvement could not explain hallucinations of this character. The stimulus caused by the organic process, whenever occurring in the visual pathways sufficient to cause a conscious recognition, must be interpreted, the author believes, in as near a manner as possible to similar objects which the stimulus may suggest. These objects, in most cases, are vague and indefinite; if persons, personal characteristics are lacking; if animals, they form in classes according to size. Again, minute details of the hallucinatory concept are lacking, showing that the hallucinations appear to be set types of objects. It is difficult to obtain exact details of their finer descriptive qualities, such as would be present in stored memory cell release. The author concludes that there is evidence at hand to show that visual hallucinations may be caused by involvement of the optic pathways from the retina to the occipital pole; that the greater proportion of the pathways lie in the thalamic temporal and occipital regions; and that

these areas are more disposed to be involved by tumor which gives the impression that they are of localizing value. However, such is the case only in proportion as to the likelihood of tumors originating in these areas of the brain structure and involving the optic pathways. The author pointed out that formed images are more likely to occur when the lesion is situated in the thalamus or the peripheral segments of the optic pathways, probably as a result of some correlative factor in the thalamus. Stimulations arising behind the thalamus in the occipital pole apparently are of only crude light or color phenomena.

DISCUSSION

DR. ALFRED GORDON: In spite of the accumulated facts concerning the pathogenesis of hallucinations; in spite of the excellent paper presented by Dr. Fay, and the perfectly legitimate effort to try to explain this on an organic basis — I feel that we are just as far advanced as we were ten years ago. First of all, in regard to diseases of the brain, there may be such a great variety of hallucinations that it is difficult to explain all hallucinations that occur in diseases of the brain in the manner that Dr. Fay, although perfectly logically, attempted to elucidate. I was interested in a case of pituitary tumor, in which hallucinations were present; the occipital lobe was not touched, and still the patient had hallucinations. It is true that any focus at the base of the brain involving the entire optic tract, from the anterior pole back to the occipital lobe may cause hallucinations. Nevertheless, in two temporal lobe tumors there was no pressure on the optic tract, and the patient had hallucinations. The tendency to explain hallucinations on an organic basis, particularly with regard to the thalamus and optic tracts, seems to be unsatisfactory. How would Dr. Fay explain hallucinations in psychoses when the brain is intact? It is true that hallucinations in psychoses have another basis; nevertheless, they are hallucinations. I am much confused with regard to the pathogenesis of hallucinations. I cannot accept the tendency of some authors to explain all hallucinations by affection of the thalamus. We are absolutely in obscurity in regard to not only the cause but also the character of hallucinations. My personal opinion is that all kinds of hallucinations are more pathogenetic than organic. The organic explanation is not at all satisfactory because it does not cover various diseases of the brain with various foci.

DR. J. HENDRIE LLOYD: Dr Fay's paper raises an interesting point. These precise phenomena are observed in epilepsy and also in migraine. They were well known in migraine, in which there is confusion of sight — what is called amblyopia; frequently there are associated with that some of these crude hallucinations, such as the fortification aura with scintillating scotoma, sometimes flashes of light, sometimes colored light, such as are observed in epilepsy. The question is sometimes discussed whether epilepsy and migraine are kindred diseases. I never believed they were, though there is some similarity. I have always thought these auras were due to cortical irritation. Dr. Fay has brought out evidence that they are not, but that they are due to irritation of the optic paths. There are other auras, however, that seem to point to a cortical origin. For instance, we sometimes have peculiar olfactory auras in the so-called uncinate type of epilepsy. In that case no doubt the discharging lesion is located in the cortical center of smell. The patient first has a horrible odor in his nose, and the next moment he goes into a fit. These large pictorial hallucinations have also been reported in migraine and epilepsy. Weir Mitchell,

years ago, reported a series of cases in migraine, and I recollect one that was reported by Gowers, in a case of epilepsy, of a little old woman in a brown or red cloak. They were very much like those Dr. Fay speaks of tonight. The only conclusion I should draw from Dr. Fay's paper is that lesions may exist in various regions of the brain in these cases; sometimes in the cortex, and sometimes in the visual paths or optic radiations. In other words, they are not limited to one place and their localizing value is not to be relied on.

Dr. Earl D. Bond: Dr. Fay's paper was interesting and excellently presented. Dr. Fay at no time tried to explain all hallucinations. One interesting point is that he has described a set of hallucinations which we can place at one end of the scale, where visual hallucinations are attended by very little emotion; on the opposite end of the scale are the hallucinations in dementia praecox, which tend to be determined almost entirely by emotion and which can often be accounted for almost entirely by the history of the patient. In between are hallucinations in alcoholic patients in different stages, in which we get combinations. We find in the alcoholic person, in addition to visual hallucinations in which he is moderately interested, auditory hallucinations with strong emotions, as illustrated by the man who claims he has not had much to drink, has always been a worthy citizen, but hears a voice calling him "a worthless sot." So I think Dr. Fay helps to line up the whole scale of hallucinations and to see the whole problem at once.

Dr. Temple Fay: In reply to Dr. Gordon, I am sure that the paper makes clear in its title, "Visual Hallucinations in Organic Diseases of the Brain," its scope and the character of hallucinations under consideration. We must make a distinction between this and any other type of hallucination. Furthermore, I have tried to point out that there was little similarity, because of the lack of definition of the objects, when compared to the hallucinations in the psychoses. I have not attempted to go into the psychotic field. It is difficult enough to try to explain what we observe in organic disease. In this attempt at analysis I have been forced to account for the fact that we have hallucinations. Why these hallucinations arise, or what are the stimuli which cause them, or are interpreted as such, it is difficult to explain. At least, we can classify them into two types, and with this classification, we find that a proportion of them are in the occipital lobe, and the great majority are confined to the temporo-occipital lobe, although hallucinations, as I have shown, may occur at any point along the visual pathways. The "formed" hallucinations, are very primitive. They are simple objects, such as a cat, dog, goat, chair or man. Occasionally, we find complex hallucinations, like a kitchen or a scene which contains more than one element. They are not comparable to those occurring in psychoses, in which many ideas and vivid scenes make up an hallucination. I want to make that distinction clear. As Dr. Bond said, we must try to start from the bottom with crude types and determine what can be established on an organic basis.

Dual Personality Apropos of a Case of Amnesia, with Analysis. Dr. Alfred Gordon.

The author discussed all psychic conditions in which the consciousness of the ego is disturbed. He discussed especially amnesia. After describing all varieties of amnesia with regard to character, duration and the occurrence of several personalities in this condition, he finally gave a detailed account of

a case. It concerned a young woman, aged 25, who, up to 1923, had lived in a continuous and highly disturbing conflict with her parents, and had no outlet for her emotions, feelings and thoughts. She finally became amnesic, and this state of loss of memory lasted an entire year. At the end of that time, following an accident, she recovered her conscious ego. All efforts to bring back to memory all the happenings during the amnesic year failed. She has, at present, no recollection of having been employed during that year, nor has she any knowledge of having married during that time. Repeated examinations failed to bring back any fact or event which occurred during that period.

In analyzing the patient's personality, the author attempted to explain the whole year's flight from the realities of life, by taking into consideration the patient's domestic situation, her relationship to her parents and all the incidents in her former life. He showed that her life was difficult, even intolerable, because of the conflict between the desire for self-expression and the sense of duty toward her parents. It was a life of intense repression, with intense protest and rebellion, and with lack of legitimate outlet. Instead of a physical self-expression, in the amnesic state the patient led the life of a personality which was real and desirable to her. In treatment, the author suggested a method for unraveling and laying bare the elements of the complex psychologic state which were in constant conflict with the patient. He also showed how to gain a better insight into the personal problems, and how the patient herself, by her own efforts, will be able to find a proper outlet for her self-expression.

DISCUSSION

Dr. J. Hendrie Lloyd: This paper is interesting and presents some important and obscure problems. In trying to discuss an obscure problem, the first thing to do is to define it. What is meant by the term, "dual personality"? It has been exploited, as we know, in recent years, and, oddly enough, it has been used for different things by different writers. Some writers who use it do not always have a very clear idea of what they mean by it. Dr. Gordon's idea is clear enough. It requires us to believe, first, in the complete abolition of memory, and that without apparent cause. Memory is one of the fundamental functions of the brain. To believe that memory could be abolished and all other faculties retained, requires us to believe a good deal. It next requires us to believe in a complete obliteration of the normal self-consciousness, that is, our sense of the ego, as Dr. Gordon calls it; and third, that that normal sense of the ego is replaced by another, or an abnormal sense of the ego. Yet, while it is abnormal, this, nevertheless, acts as a normal self-consciousness. You must be something of a psychologist to get all that into your head, and especially to believe it. It requires us to believe in the complete erasure of the sense of personal identity. If we stop to think, that means the blotting out of the whole contents of one's mind from the time one is born until the time the event occurred. And then something else is put into you — another consciousness, another personal identity. I find it hard to believe all this. I can understand, I think, the grounds on which the theory has been built up, and I want to speak briefly of these. There are various states in which self-consciousness is affected. In sleep, self-consciousness is abolished, but our sense of personal identity is only in abeyance. When we wake up we know ourselves at once. A dream is hard to explain, but while it does to an extent approach this condition of double consciousness, it is not exactly like it, because during a dream we do not lose our sense of identity. Whatever

fantasy we pass through it is always our self that is dreaming. We wake up in the morning and recognize that fact. It is not a case of dual personality; it is a case of disturbed personality. So, in the delirium of fever; a man goes through a bad attack of typhoid fever and is out of his mind for a week or two. His self-consciousness or sense of the ego is much disturbed, but there is nothing duplex about it. He comes out of the fever, and the period of his delirium is absolutely blank to him; and he will never be able to recall it because all his mental factors were obscured by delirium; but his sense of identity is not disturbed. He recognizes fully that he was simply delirious. Then next is the state of insane delusion. I can recall a case at the Philadelphia Hospital a number of years ago, of a man who believed that he was the Messiah. He dressed himself like a Messiah; he had long hair over his shoulders, and looked something like the conventional pictures of the Messiah. He had his picture painted, and I have one of his photographs at home. The man was under profound religious delusion. In a sense, his personal ego was overthrown, but it was not double, although he had lost all critical sense of his own personality and believed he was another personality, as different from himself as well could be. That is the point. If we suppose the man had recovered, he would not have had a break in his memory, but would have fully recognized that he had been living in an insane delusion.

Now we come finally to what I think to be the core of the matter, that is, hysteria. Hysterical psychoneurosis, I think, is the explanation of these cases. I think the only double personality is one personality in the patient and another in the doctor. In other words, a great deal of their mental state is put into them, often unconsciously, by suggestion; it may be suggestion from without or from within, that is, autosuggestion. A hysterical person, to a certain extent, is an actor. On the stage an actor throws himself into a new character. I have heard it said that the best actor is so completely immersed in the part he is acting that for the time being he seems to himself to be the part. I can imagine that a person acting on the stage might become thus immersed and lose his own identity, temporarily, of course. That is, to a certain extent, what takes place in hysteria. I am not much of a freudian, but I think there is a freudian explanation for all this. These people are often under some moral stress or strain that makes it necessary for them to try to repress their emotions. They are suffering under repressed emotions; they have had extremely disagreeable experiences in their environment and try to put them out of their lives, and in doing that they present a so-called double personality. This was preeminently so in Dr. Gordon's case. The patient built up an elaborate "defense reaction," as it is called. I think we should try to see whether anything in the patient's history would justify us in believing there had been some extremely personal emotional condition which the patient had been trying to shove aside and into the subconscious. Dr. Gordon has given a graphic description of such a depressing emotion. The woman was accused of stealing money. Dr. Gordon passed rather lightly over that. I did not quite understand whether she was convicted or only accused. But suppose she was not guilty; nevertheless, she was accused and threatened with arrest. A person under such circumstances might find it convenient to step out of her own ego into some other ego where the police could not catch her. The woman, in other words, had a strong motive for putting on, as it were, this appearance of another personality than her own.

This is not a new idea, this idea of dissociated or discontinued personality. It is very old. The ancient Greeks were great speculators about such problems, and one of the speculations of Plato was about the immortality of the soul. Plato proposed this theory: "Yes, we are immortal, but at the time of death the soul is re-absorbed into the Divine Essence" (whatever he means by that) "and it loses its personal identity." It has become immortal because it is absorbed into the Deity. It retains no memory of ever having been embodied in a mortal man. In other words, you are immortal, but you have lost your personal identity and all memory of it.

Of course, the idea is entirely preposterous and self-contradictory. You can have no idea of immortality unless you preserve your personal identity. I speak of this only to show that the old Greeks made this kind of speculation. There are hardly any mental twists or turns that they did not speculate about 2,000 years ago, and among other things they speculated about double personality, this break in the sense of personal identity.

Dr. Alfred Gordon: Evidently Dr. Lloyd admits on one hand that in amnesia there is something wrong with the person. He calls it disturbed personality. It is a question of terms. Dr. Lloyd's comparison of an amnesic person with an actor is inadequate. An actor is perfectly conscious of what he is doing, and does his work intentionally, but the amnesic person does not know he is under the exclusive influence of subconscious elements. Dr. Lloyd does not like that term, but I must use it. As to the possibility of hysteria in this case, are we going to call every case of that kind hysteria? Amnesia is a fact. We know there are organic lesions in which the patient loses his memory. I know of a patient who, instead of going to his office, took a train and wandered off to Baltimore. A hysteric attack would hardly lead him to take a train for Baltimore instead of going to his office in Philadelphia. Amnesia is a real disturbance of personality. We almost daily read in the papers that a person was found without memory, when there could be no special motive for that, in another city.

Dr. Lloyd alluded to the theft in this case; hence, he says, there is a possibility of a fraud. There are cases in which there can be no consideration of fraud or of money, and yet the patient is amnesic. In this particular case the young woman did not have the money. It was definitely shown later that she did not take the money, and the fact that there happened to be a theft or stealing does not mean that the amnesic phenomenon is fraud.

Dr. Lloyd also mentioned Freud. He does not like Freud's teaching; nevertheless, we must admit that in all psychoneuroses the principle of Freud is correct. The latter proves that there is in us a set of forces more powerful than the conscious ones, and the latter are controlled by the former.

The present case is genuine because the patient was under observation not only by myself but also by Dr. Manning, who has been a friend of the family for years, and we have continuously watched the case and noted the complete lapse of memory. Dr. Lloyd objects to the term "dual personality." Call it what you will, but there was something different in the same person that had not existed before. I believe that the explanation of this amnesia lies in the urge of getting away from an unpleasant situation subconsciously. She was in continual conflict for years and years. She had her own emotions and feelings, but no outlet. Being psychoneurotic, she endeavored to dissociate herself from the real life, hence her amnesia.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, March 26, 1926

WILLIAM G. SPILLER, M.D., *President, in the Chair*

REPORT OF A CASE OF CHOREA IN THE SEVENTH DECADE WITH APPARENT RECOVERY. DR. ALBERT C. BUCKLEY.

The patient, a woman, aged 69, whose parents were first cousins, was married at 17, and had six children, of whom three died of acute illness in early life, one died of diphtheria at 12 years, and two are living adults in good health. At the age of 25, the patient was shocked by the death of her two brothers from diphtheria on the same day. She had suffered no illnesses, but had not been strong since the menopause and had had a good deal of "rheumatism." About three months prior to admission to the hospital, May 28, 1925, it was noticed that she was becoming "nervous"; the condition grew gradually worse, and was shown by kicking movements of the right foot, movements of the jaws accompanied by a smacking sound and silly laughter without apparent cause. On admission the movements described were present, and in addition there were purposeless movements of the right hand and arm; at times the arm movements described arcs. There was general restlessness and the patient moved about in bed in an awkward manner.

Examination.—The patient presented a dull, expressionless appearance when the face was at rest, and was of the thin, wiry type. The right lobe of the thyroid was enlarged, apparently cystic. No cranial nerve involvement was observed. Inspirations were arrhythmic and jerky and averaged 28 per minute. Loud, blowing, systolic murmurs were present. The radial and temporal arteries were sclerotic; the pulse was 108, irregular and intermittent. The blood pressure was systolic 140, diastolic 66.

Station and gait were unsteady; the dynamometer reading was: right, 100; left, 130. The tendon reflexes were active but not exaggerated. The arms could not be held steadily when extended.

At the end of about six weeks the movements were less marked, although there were still "unnecessary movements of the lips, tongue and jaws, and irregular, involuntary movements of the right hand at times." Speech was little if at all affected, except that there was the usual mouthing and chewing of words characteristic of other choreas, so that there was no distinct dysarthria. Writing was difficult on account of the motor disorder. Mentally the patient was dull but without confusion; emotional instability was occasionally observed.

When the patient first came under observation, the disorder was regarded as of arteriosclerotic origin (softening), involving the corpus striatum, and it was expected that the symptoms would persist and follow the usual course of such a lesion. Before the end of the third month, however, improvement occurred to the extent that all choreiform movements had disappeared, and the patient had gained considerable weight, and complained only of tiring easily.

At the time of this presentation, nearly six months after the patient's discharge from the hospital, there has been no return of the movements.

DISCUSSION

DR. J. H. LLOYD: I think that this case is a form of senile chorea due to impaired circulation through the basal ganglia, especially the putamen in the lenticular nucleus. I reported such a case. It began suddenly with violent

choreic movements on the opposite side of the body. The patient died in a few weeks, and a lesion was found in the putamen on the opposite side. This man, like Dr. Buckley's patient, also had a tendency to explosive laughter, such as is seen in pseudobulbar palsy.

Dr. A. C. Buckley: Dr. Mills, regretting that he could not be here, wanted me to say that he has had cases, at least two he thought, of chorea in the senile period with recovery, and he believes that there is no reason why transitory disturbances based on arteriosclerosis should not give rise to functional choreiform syndromes.

Differences in Muscle Contraction in Central and Peripheral Facial Palsy. Dr. A. M. Ornsteen.

A number of cases of recovered facial palsies of peripheral type in which there were associated movements and secondary contractures were shown on the moving picture screen. It was pointed out that the associated movements in the orbicularis oris and the orbicularis palpebrarum are due to a regeneration of nerve fibers from nuclear cells of one muscle to the other muscle and vice versa; i. e., cells in the facial nucleus formerly supplying only one of the muscles referred to now innervate both muscles so that every time one is innervated the other participates in the movement. Such muscles do not have the same volitional power as before. This explanation for associated movements following Bell's palsies has been recognized and described by several authorities, but the following explanation of the secondary contractures was first given by Dr. W. G. Spiller, who states that because of the double innervation, these muscles never completely relax, and that the continual overstimulation results in secondary shortening and contracture.

Two cases of apparent contracture in hemiplegic patients were shown in contrast to a true contracture around the mouth in the peripheral type cases. In the central cases there was, of course, no involvement of the orbicularis palpebrarum and there was no associated movement between these two muscles. There was, however, an associated movement of the muscles about the mouth with each volitional movement of the partially paralyzed upper extremity. As a result of the associated movement, the muscles about the mouth appeared to be in a state of contracture which disappeared after cessation of volitional movement of the arm and thus differed from the contracture in the Bell's cases, which is permanent. In the central cases emotional factors also produce a pseudocontracture of the affected side of the mouth.

In these two types of cases we find associated movements, in the one type as the result of faulty regeneration of peripheral nerve fibers and in the second type due to a release of automatic mechanisms secondary to interruption of the corticospinal motor tracts.

Multiple Lesions of the Cord. Dr. J. A. Reisinger.

A man, aged 47, was admitted to the neurosurgical ward of the University Hospital, Jan. 27, 1926, with the chief complaints of pain in the back and weakness of the lower limbs. He stated that at the age of 12, he was struck in the back by a log and as a result was confined to his bed for some time though he was not paralyzed. He apparently recovered completely from this and had no further trouble with his back except for occasional attacks of lumbago. The present symptoms date from March, 1925, when he twisted himself while at work. At this time he was seized with a sudden sharp pain

that crossed the abdomen below the umbilicus. Since the injury the patient has had pain whenever he twisted his body, flexed his head, coughed, sneezed or jolted himself in walking, but he was able to work in spite of the pain until the middle of December when he first entered a hospital. At present he has little discomfort.

Early in December, he noticed for the first time that his right hand was weak and that his little finger was cold and numb. In the middle of December he entered a hospital in Pittsburgh, where his back was placed in a plaster of paris cast for two weeks, the diagnosis being Potts' disease. The cast gave no relief, and since, he has been so weak in his lower limbs that he cannot walk without support.

Examination.—The man was well developed and well nourished, but unable to stand or walk without support. Mentally he was clear. The head and neck gave negative findings. The pupils were small and equal, and responded poorly to light. The thorax presented a rounded kyphosis in the lower thoracic region and an irregular scoliosis of the whole spine. The heart and lungs were normal. The dynamometer reading in the right hand was 200 and in the left hand 350. He was able to perform all movements with both hands although somewhat awkwardly with the right, but could not approximate the thumb and fifth finger of this hand easily. He showed no dysmetria except for the weakness in the right arm, no adiadokokinesis and no astereognosis. The biceps and triceps reflexes on the right side were 1, and on the left side 2½. The lower limbs were weak, but the patient was able to perform all movements including fanning of the toes, and he could stand and take a step with support. The ability to place the heel to knee was perfect on both sides. The patellar reflexes on both sides were 3. There was a positive Babinski sign and ankle clonus on both sides. The abdominal reflexes were absent.

The sense of vibration was impaired up to the pelvis and the sense of position in the great toe was disturbed. Tactile sensation was intact over the entire body except for the little finger of the right hand. Pain and temperature sensations were impaired or absent on the right upper and the left lower extremity, and on the left side of the trunk to about the fourth dorsal segment. On the thorax there was loss of the same sensations on the right side continuous with that of the right arm and extending down to the sixth dorsal segment.

Course.—Lumbar puncture was done and a Queckenstedt test revealed complete block of the subarachnoid space. Following this procedure the signs in the lower extremities changed considerably so that one week after his first examination, he was unable to move his lower limbs and could barely flex his toes. The sensory picture changed also so that pain and temperature senses were absent or greatly impaired and the condition of the upper extremities and thorax had not changed.

There was no bladder or rectal involvement until February 17, when he became incontinent of urine at night.

The blood and spinal fluid tests for syphilis were negative. Roentgenograms of the spine showed destruction with collapsing of the body of the eleventh thoracic vertebra, but without encroachment on the spinal canal. The bodies of the vertebrae were everywhere flattened and there was a moderate amount of hypertrophic spondilitis, not of tuberculous appearance; it may be a metastatic growth, a primary sarcoma, syphilis or possibly trauma.

CEREBRAL HEMORRHAGE IN PERNICIOUS ANEMIA. DR. J. H. LLOYD.

The patient, a married woman, aged 24, had one living child and had had four miscarriages. On February 5, in her fifth pregnancy, she had her fourth miscarriage and was confined to bed with headache, occasional chilly feeling and probably some fever. On the ninth day after the miscarriage she had a convulsion; she was admitted to the Methodist Hospital on the next day, in Dr. Piersol's service. Her personal history was unimportant except for the frequent miscarriages, and the fact, as reported by the husband, that for some months she had been growing very pale. No cause could be determined for the miscarriages, and they may possibly have been self induced. The spinal fluid Wassermann test was negative, globulin was not increased and there were but 3 cells to the cubic millimeter. The patient had no detectable syphilitic stigmas, and the pupils reacted normally to light and in accommodation. The husband denied infection with syphilis. There had not been much loss of blood following the miscarriage. The urine at all times showed a slight trace of albumin, but was otherwise normal.

The patient's appearance was striking, she was obese and very pallid, with little or no color in the lips, sclera or conjunctiva. The first blood count showed: hemoglobin, 38; red cells, 1,800,000; white cells, 14,500. There were no poikilocytosis, nucleated red cells or other significant changes. Blood transfusion was done February 16; on the next day the hemoglobin was 33; the red cells had increased to 2,430,000; white cells to 16,350.

On February 19, two weeks after the miscarriage, the patient began to have frequent convulsions, which were confined to the right side and associated with right hemiplegia, partial aphasia and hebetude. The neurologic examination was made on the following day, and the opinion was given that there was a left sided cerebral lesion, probably thrombotic and apparently due to the extreme anemia.

The next blood count showed that the hemoglobin had fallen to 30 the red cells to 1,630,000 and the white cells to 8,700. Another transfusion was then done. The convulsions recurred every day, lasted longer (one of them for eighteen minutes) and had to be controlled with ether. The hemiplegia seemed at times not to be complete. The patient failed rapidly and died, February 23, on the eighteenth day after the miscarriage.

Necropsy Findings.—The lesion was a blood-stained area, 4 or 5 cm. in diameter, in the left parietal lobe, bounded in front by the fissure of Rolando. There was evidently destruction of brain tissue, but little if any free hemorrhage or clotting. A bunch of veins in the dura, just over the lesion, was markedly thrombosed, but Dr. Richardson, the pathologist, tells me there was no thrombus in the superior longitudinal sinus. The initial lesion seemed to have been a venous thrombosis.

The nature of the anemia, and its relation to the lesion in the brain, are the interesting points. It seems to have been a secondary anemia, but its cause was not determined by the necropsy or by the history of the case. The husband was definite that the patient had been growing pale for some months; profuse hemorrhage after the miscarriage was denied. The blood picture was not that of pernicious anemia. I thought of a possible chlorosis, as the patient was only 24 years of age. Also of a tapeworm infestation, especially with bothriocephalus, but no tapeworm was found.

Thrombosis of the sinuses of the brain has been observed in some forms of anemia, especially in chlorosis. It seems to be rare in pernicious anemia.

In the pathologic records at Blockley there are only six cases of pernicious anemia, in two of which there are recorded slight areas of softening.

The extreme obesity of the patient is noteworthy. She did not present the appearance of the Fröhlich syndrome, but when I saw her it was difficult, because of her extreme illness, to make a satisfactory examination. The blood sugar was increased. The basal metabolism was not determined. No lesion of the hypophysis was found at necropsy.

ASTEREOGNOSIS. DR. ALFRED GORDON.

A man, aged 45, two weeks ago suddenly felt numbness in his left hand so that he could not button his overcoat. At the same time he noticed that his face was drawn to the right side.

Examination.—The power of the left arm and hand is intact, but when he is asked to extend the fingers, the left hand presents some flexion of the fingers while on the right side the fingers are fully extended. There is no paralysis as the fingers are moved in all directions, but there is a marked awkwardness in the left hand, especially for fine acts. He is unable to carry out correctly any act in which assistance of the left hand is needed. There is some dysmetria in the left hand in the finger-to-nose test. The objective sensibilities present some changes, although touch and pain are preserved. Temperature sense is somewhat altered; when extreme heat and cold are applied to the left hand or forearm, the patient feels them more keenly on the left than on the right side. Tests for deep sensibilities show some slight alterations in the sense of position; there are also some errors in the compass test. All the sensory changes are slight.

The most pronounced disorder is in the stereognostic sense; the patient frequently makes gross errors in recognizing objects and their consistence. Sometimes he is able to name an object, but only after considerable delay.

He complains of gross awkwardness and at times of absolute inability to hold objects between his fingers; they drop out of his hand; he has difficulty in tying his scarf, and in finding a buttonhole in his shirt or coat. The power of the individual segments of the left upper extremity is preserved and the biceps and triceps reflexes are present and normal. The left knee jerk is somewhat increased but equally so is the right knee jerk. There is no ankle clonus but the plantar reflex is in extension only with Oppenheim's and Gordon's methods, not with Babinski's. Sensation in the lower extremities is normal.

Another striking peculiarity in this case is the involvement of the left lower half of the face; it is deviated to the right side. The palsy is quite pronounced, as at first it gives the impression of a peripheral facial palsy. Superficial sensation of the face is slightly diminished. Further examination shows that the cardiac apex is in the seventh intercostal space and lies external to the mamillary line. The second aortic sound is markedly accentuated. The urine is normal, and the blood Wassermann reaction is negative.

The patient had an identical attack on the same side six months ago, from which he made a total recovery. Each of these attacks developed suddenly without loss of consciousness and they were not preceded by untoward symptoms such as vertigo or headache.

Comment.—The clinical picture of this case consists of motor symptoms in the form of left lower facial palsy and of a sensory symptom in the form of astereognosis of the left hand. The localization of these two disorders presents some difficulty. The character of the sensory disorders, especially the involvement of the deep sensations with predominance of the stereognostic

disturbance presupposes a cortical involvement. Had it not been for the involvement of the face, the superior parietal lobule could have been incriminated. The motor involvement of the lower face leads to its localization in the lower portion of the rolandic area. Redlich (1893) and Von Monakow (1898) localized disturbances of deep sensations, including astereognosis, in the lower parietal lobe, especially in the supramarginal gyrus. The largest number of Redlich's cases contained lesions of the ascending parietal convolution especially in its postero-inferior portion. As is well known, the latter is supplied by the same arterial branch as the supramarginal gyrus. If we are to assume in the present case only one lesion, we must admit that the lower halves of both ascending convolutions are involved. It will explain the lower facial paralysis and, according to Redlich's findings, also the astereognosis. This consideration opens the question of the function of both ascending convolutions. While it is true that modern researches on the architectonic structure of the cells of these two convolutions show a decided difference and consequently point to a difference in function, one cannot avoid referring to Horsley's observation (1909) according to which extirpation of the ascending frontal convolution was followed by hemiplegia and involvement of the muscular sense of tactile localization and of stereognostic sense. The present case favors the idea of one lesion involving simultaneously the two lower thirds of both ascending convolutions; namely, the centers of the face and arm. It favors the localization of the center of the deep sensibilities, particularly of astereognosis, either in the ascending parietal or in the supramarginal gyrus which is irrigated by the same arterial supply as the ascending parietal. It points to a possible correctness of Redlich's view concerning the localization of astereognosis. At all events one may say that the superior parietal lobule is not the only cortical center for cerebral stereognostic perception. One may, however, also admit, in cases of astereognosis in which other portions of the cortex were involved, the possibility that the intracortical association fibers connecting the superior parietal lobule with other portions of the cortex may have been affected. From this standpoint the superior parietal lobule remains the chief center for deep sensibilities.

As to the nature of the lesion in this case, in view of the patient's cardiovascular condition, there may have been either an embolic lesion or an angiospasm. The rapid and total disappearance of the symptoms after the first attack favors the idea of an arterial spasm. The longer duration of the second attack renders the prognosis more guarded. In the *Journal of Nervous & Mental Disease,* (August, 1914) I reported eight such cases with necropsy findings. Each patient had a series of attacks of transient hemiparesis, occurring at different intervals during life. It was noticed that with each subsequent attack the paralytic condition increased and lasted longer so that eventually a permanent hemiplegia became established. It was evident that the intermittent spasmodic contraction of the cerebral blood vessels gradually led to a destruction of the tissue supplied by them through a process of softening.

In the present case, we are dealing with a similar condition. The present attack seems to be quite serious in view of its persistence and duration. A softening of the cortical tissue is evidently taking place and this renders the prognosis unfavorable. The present case leads to a consideration of another special feature. It has already been pointed out that astereognosis was pronounced while the position, tactile localization and the compass points senses were slightly disturbed. If a manual recognition of an object and of its consistence is dependent entirely on the integrity of different modes of sensibilities, deep and superficial, it seems singular that in this case all superficial sensations,

touch, pain and temperature, are preserved and a few deep sensibilities, such as position and compass sense are but slightly involved. The patient makes few and only occasional errors in the tactile localization. The present case, in which the stereognostic preception is grossly involved, indicates the possibility of the existence of a certain form of astereognosis which is independent from other sensory disturbances. This is the so-called "asymbolia" of Wernicke and of Claparède.

DISCUSSION

Dr. Temple Fay: The work of Head regarding the parietal lobe as associated with certain motor disturbances will probably explain this case. Head called attention to the fact that lesions in the parietal lobe caused sufficient sensory disturbance to produce apparent motor changes, and the case of Dr. Gordon also falls into the segmental type. I do not consider it necessary to attempt to explain the condition by a dual lesion. I recall a case in which a man had received an injury with a crowbar over the left parietal lobe. The point of the bar had caused a depression of the inner table of the skull, so that a spicule of bone protruded into the parietal lobe, close to its upper margin. In addition to astereognosis in the right hand, this man had spasticity of the index finger and thumb of the right hand, and it was felt that, though the roentgen ray showed involvement high up in the parietal region, he probably suffered from a hemorrhage which had caused scar tissue formation and injury to the hand center which is supposed to be in the prerolandic area, in front and below the roentgen-ray evidence of injury. For this reason I performed craniotomy to disclose the motor area as well as the site of the injury, and at operation there was only gross injury to the brain structure at the points of bony protrusion of the inner table in the parietal lobe. This consisted of a small depressed area of destruction, about the size of a twenty-five cent piece, with adhesion of the dura to the pia-arachnoid. The spicule of bone was removed, the dural adhesions were freed, and silver clips were placed about the margin of the injury on the cortex, so as to show definitely by roentgen ray later the site of actual cortical involvement.

The fact that the man's function in his index finger and thumb greatly improved after operation appears to be conclusive evidence that the region of the parietal lobe was responsible for the motor involvement. As this operation disclosed only one lesion instead of two, as had been anticipated, and as the parietal lobe was the site of involvement, I feel that this case is similar to the one Dr. Gordon presents, and therefore could be explained on a single lesion.

Dr. A. M. Ornsteen: An interesting observation of Head's relative to localized parietal cortex is that the sensory defect is sometimes confined to several fingers of one hand simulating peripheral nerve patterns, so that a cursory examination may mislead one to consider the sensory loss to be of peripheral nerve origin. The case referred to by Dr. Fay presented the characteristic parietal sensory picture in the thumb, index and middle fingers only.

Muscular Atrophy. Dr. F. H. Leavitt.

This paper will be published in full elsewhere.

Structure and Connections of the Substantia Nigra. Dr. Amando Ferraro.

Book Reviews

AN INTRODUCTION TO OBJECTIVE PSYCHOPATHOLOGY. By G. V. HAMILTON. St. Louis: C. V. Mosby Company, 1925.

The author states that the book is essentially an account of his studies and interpretations of various modes of human and animal behavior; and there is a foreword written by Robert M. Yerkes hailing this book as "the first chapter of a new and promising psychopathology." The introduction, written for "both medical and non-medical readers" (the reviewer would say rather the latter than the former) describes some of the fundamental biologic data as applied to medical and psychologic investigation, together with a statement of a method of research to determine "how the human organism tends to respond to the great variety of stimulations which call for adjustments of the body as a whole to the outside world" by a program aiming: "(1) to isolate a few of the more important types of situations to which the nervous patient is apt to respond abnormally; (2) to subject various mammalian species to such stimulations, to study their methods of response thereto, and to isolate, if possible, responsive properties (reactive tendencies) which are common features in the human organization and in various infrahuman species; (3) to include children and adult human subjects in comparative studies of behavior; (4) once a given reactive tendency has been isolated, to explore for the principles which govern its modification by experience."

As "Baffling disadvantage seemed . . . . to be the most general type of stimulation to which the nervous patient is apt to manifest abnormal responsiveness, . . . a good deal of time was devoted to . . . . studying the reactions of monkeys to sexual and nonsexual stimulation." The results of these studies were later compared with studies concerning "Two Hundred Nervous Cases" which are described in varying degrees of detail in the second chapter.

The third chapter is a summary of the survey findings in a town of 30,000 inhabitants relative to the two hundred cases. (One hundred and forty-five of the persons involved) "seemed to owe their nervousness wholly or in part to maladaptive habits of response to personal problems or difficulties;" many of them "not only presented troublesome nervous symptoms which seemed to have been thus determined, but were suffering from acute physical disease of one sort or another;" they are described as: (1) cases presenting pathologic types of reactions to stimulations which evoked adjustments of the organism as a whole; (2) neurologic and other cases in which there were no significant pathologic reactions of the organism as a whole. There follow statistical tables relative to the distribution of the cases according to sex, age, civil state and occupation.

The author's "constructive summing up of the therapeutic findings . . . . demonstrated the practical value of explaining the patient's illness to him in objectively formulated principles," and led him to adopt the following procedures in dealing with nervous patients: prevent the patient from feeling on the defensive, and require him to give a complete list of his discomforts and disabilities; obtain records from physicians in other fields of medicine "who may be responsible for disclosing any tangible physical disorders which may be present"; hold the patient to a strictly orderly account of himself by being constantly reminded that the most important question is "To what things are you now responding inadequately, and how are you responding to them?"

Following this, the author asks himself three general questions: (*a*) Is this patient reacting persistently, nonadjustively and affectively to baffling disadvantages of one sort or another? (*b*) Is he reacting directly to his personal problems or is he inhibiting direct responsiveness to them and disclosing in consequence indirect reactions to such behavior? (*c*) Does his present behavior, when correlated with known or suspected past experiences, suggest the presence of significant conditioned reactions?

While the author states on two occasions that his patients knew nothing about psychanalysis or the freudian theory, ten pages are devoted to a recital of the author's statement to a patient who had "read extensively in psychoanalysis"; this section is a review of freudian and neofreudian doctrines. The reason for this is not clear to the reviewer, unless it serves to compare the method of the author (Hamilton) with those of the psychanalytic school, as he discusses the doctrine of "the unconscious" and its terminology.

In part II, "The Principles of Objective Psychopathology," emphasis is placed on one of the objects of the book, namely, to persuade the internist that he need not depart from the fundamental methods, concepts, terminologies and sense-organ orientations of the natural sciences in order to employ the same degree of scientific purposefulness in dealing with his nervous patients that he employs with all other classes of patients. The following pages contain a discussion of some of the psychologic views, especially those of the behavioristic school, and the author concludes that he "can see no other safe ground for the psychopathologist than that upon which the surgeon and internist stand in classifying as mental only those reactions which the patient reports as direct experience."

Chapter V, on "The Foundations of Psychopathology," states that the book "is exclusively concerned with kinds of nervousness that are not due to any known infections, intoxications or structural changes in the nervous system, that do not require institutional management and that the internist ought, with few exceptions, to accept as coming within his general field of therapeutic and diagnostic endeavor." After again referring to the freudian principles, we are told that, in the opinion of the author, "it is possible to abandon unverifiable psychomorphic interpretations of nervousness without thereby sacrificing anything of value that psychoanalysis has to offer."

Chapter VI contains brief statements concerning neural morphology, physiology and endocrinology.

In Chapter VII, the problem is stated as: "what types of reaction to baffling situations do mammals in general — both human and infrahuman — present when confronted by baffling disadvantages? What light, if any, would such information throw upon the maladjustive reactions of nervous patients?"

Experiments on human subjects, infrahuman and other mammalian animals gave results as follows: "a mammalian's first or first few encounters with an unfamiliar or baffling type of disadvantage usually evoke . . . . instinctive responses. In addition, the subjects disclosed . . . . five different general types of reaction. . . . . Only one . . . . could be classified as rational adaptation." The author makes the summarizing statement: "When a Disadvantage is of a kind to act over longer periods of time, and is too subtle to be adequately met by affectively reinforced instinctive modes of response, there must be developed a habit of reacting rationally thereto if the individual is to escape nervousness."

Chapter VIII, habit formation, deals with the neurologic explanation of habits, behavioristic principles, and the abandonment of nonadjustive movements. Two human examples are used to illustrate the behavioristic point

of view and described as the "Two Housewives," one trying to adjust herself to the problem of doing without a servant; the other in her endeavor to adjust herself to an "incorrigibly adulterous husband." "Twenty-three of the patients in the survey owed their nervousness wholly or in part to persistent, non-adjustive, affective reactions to baffling, somatic disabilities." "One's ability to effect a cure . . . . is often contained in the possibility of enabling the patient to develop habits of rational responsiveness to situations which have previously elicited infrarational, more primitive and — by reason of their affective components — pathogenic reactions."

Chapter IX is concerned with "The Relation of Inhibition of Responsiveness to Indirect Responsiveness." Chapter X deals with "Unsatisfied Major Cravings" and begins with Thorndyke's principle of readiness, which is used to account for the prepared state of organisms for response which enables them or "impels them to engage in activities which are likely to satisfy corresponding basic needs." Cannon's work is also utilized in the establishment of the author's "present formulation."

Chapter XI deals with "Reactions to Inferiority" and refers to the views of Adler and Kempf on the "inferiority complex." Next appears a behavioristic evaluation of inferiority reactions, the author's views having "been determined by comparative studies of mammalian adjustments to inferiority, including those of the nervous patient." A behavioristic explanation of why patients react as they do to their inferiorities does not appear, nor do "the explanatory guesses of the psychoanalyist afford me much greater enlightenment . . . ."

Chapter XII discusses sexual behavior and after referring to the freudian sexual theory, the matter of prepubertal sexual tendencies is considered; the author states that he has "followed Freud's presentations of fact as closely as my own experience and convictions will permit, but I have limited myself to that which I have been able to check by my own experimental and other kinds of observation."

The general trend of Hamilton's work shows an attempt to harmonize the observations of the psychogenic school of psychopathologists with those of the behaviorist, and to give reasons for the existence of the phenomena on a basis which can be studied by objective methods. To the reviewer, the task would seem commendable, although the "psychanalytic pendulum" has coursed through its widest excursion, and appears to be in the process of settling into an arc of smaller dimensions. There still appears to be ample ground for assuming that mental phenomena cannot be fruitfully studied entirely from an objective standpoint. One need not be a behaviorist, however, to be interested in the volume, as it contains much that can be used by practicing psychiatrists.

REPORT OF A MENTAL HEALTH SURVEY OF STATEN ISLAND (THE BOROUGH OF RICHMOND), NEW YORK CITY BY THE NATIONAL COMMITTEE FOR MENTAL HYGIENE, JANUARY-APRIL, 1924. EDITH R. SPAULDING, M.D. Paper. Pp. 100. Utica, N. Y.: The State Hospitals Press, 1925.

At the request of representative citizens of Staten Island, the National Committee for Mental Hygiene conducted a survey of what is being done in that community "to decrease mental disease, prevent delinquency and criminality, protect the feebleminded, lessen dependency, and help solve its problems of social maladjustment and social inefficiency." This book contains a report of the conditions found, together with recommendations for measures to meet them. Some of the facts are striking, even startling, and are well worth the serious consideration of all interested in mental health and com-

munity welfare. It was found that one in every seventy-three children passed through the children's court in one year; one in every 167 persons served time in the county jail; one of every 332 residents of the borough was a patient in a state hospital for mental diseases; one in every ten school children needed help of a mental-health service for some form of mental, nervous, physical, emotional, personality, educational or social difficulty. Of 2,340 children studied in the public schools, 3.6 per cent were feebleminded, 9.2 were borderline mental defectives, and 16.9 were dullards.

The principal recommendations concern: the need for the establishment of means for recognizing and dealing promptly with abnormal mental conditions by the establishment of mental hygiene clinics for the study and treatment of all persons presenting behavior or personality disorders; the routine, periodic medical examination of all school children; extensive enlargement of special-class facilities in the schools; the establishment of probationary schools for special behavior cases; the provision of mental wards in general hospitals for the prompt care and treatment of acute mental disorders, and the development of psychiatric social service.

The figures given amply illustrate the need for these recommendations, none of which is new. The principal difficulty in the way of carrying them out, however, lies in the lack of trained personnel, a lack that should be called earnestly to the attention of universities and medical schools. Survey after survey has established the need; the present report emphasizes it to a marked degree.

Ueber Genese und Behandlung der exsudativen Paroxysmen. By G. C. Bolten. Volume 31 of the "Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten, Beihefte zur Monatsschrift für Psychiatrie und Neurologie" edited by K. Bonhoeffer. Price, Mk. 5.70. Pp. 110. Berlin: S. Karger, 1925.

Under the heading of the "exudative syndrome" are discussed: Czerny's exudative diathesis, acute angioneurotic edema of the skin (Quincke's disease and its equivalents), acute edema of the mucous membranes, urticaria, the angioneurotic form of acute cerebral edema, genuine asthma, genuine epilepsy, experimental and postoperative epilepsy, genuine migraine, mucous colitis (enteritis membranacea) and dysmenorrhea. Before describing what he calls the special pathology of the exudative syndrome, Bolten reviews critically the various theories of the formation of lymph, Widal's conception of crise hémoclasique, choc protéopexique, anaphylaxis and idiosyncrasy, Abderhalden's investigations of the body ferments, the metabolic disturbances during the paroxysms of the exudative syndrome, the vasomotor trophic disorders, the vegetative stigmata (oculocardiac reflex and eosinophilia) and the relationship of all of these to the syndrome.

Bolten's principal conclusions are: 1. The various exudative paroxysms are genetically identical with each other; they show merely morphologic differences in the congenital predisposition of the organs of the persons afflicted. The genetic relationship of the paroxysms to anaphylaxis is slight. The exudative manifestations themselves are evidences of the reaction of the organism to certain toxic substances and also the means of getting rid of them. In the genuine exudative syndromes the toxic substances are endogenous in origin, whereas in the idiosyncrasies they are exogenous. 2. The chemical composition of these toxic substances is unknown, although it is known that they represent the intermediary products of the albumin-nuclein-fat metabolism; it may also be considered as established that some of the metabolic products

of the cells of predisposed persons are also toxic, and that these toxic products consist on the one hand of colloidal proteins, and of acids (lactic and amino-acids) on the other. 3. The source of origin of these various toxic products is the intermediary metabolism during which the formation of the products of decomposition is delayed, such delay being due to a diminished activity (perhaps also a diminished formation) of the different ferments. 4. The liver has little to do with these ferments, so that the crise hémoclasique is not a reliable index of hepatic insufficiency, and it certainly is no evidence of the proteopexic function of the liver. The diagnostic value of the crise hémoclasique is still very doubtful; leukopenia is of little clinical significance because it may be entirely physiologic. 5. The cause of the delayed metabolism must be sought in a congenital hypofunction of the chromaffin system and of the thyroid with a resulting hypotonia of the entire sympathetic nervous system. 6. The vasomotor and trophic disturbances encountered in the syndrome are the direct results of this sympathetico-hypotonia; these disturbances may at the same time be in direct causal relationship with an insufficiency of the endocrine system which may to a certain extent be associated with the exudative manifestations. 7. The increased eosinophilia is evidence of a chronic autointoxication; the "gout curve" of the uric acid excretion in these patients would seem to point to a diminished nuclease effect (a large group of ferments which gradually breaks down the purin bases). 8. The exudative (angioneurotic) paroxysms are best combated by the administration of hormones, especially preparations of the so-called accelerating endocrine glands.

This is Bolten's thesis. He is apparently much more certain of the correctness of his conclusions than his arguments in the text would warrant. In the reviewer's opinion the conclusions, ingenious as they are, are based altogether too much on circumstantial evidence. He makes many statements that are not based on facts as yet established — at least to the satisfaction of critical students of this problem. This is particularly true as regards the endocrines and the results of chemical investigations carried out in test tubes and on experimental animals. All in all, the monograph is an excellent review of the subject, although it must be admitted that it contains nothing not already well known to American physicians who keep abreast of the general medical literature of the day.

J. Hughlings Jackson: Eine Studie über Krämpfe (1869). Übersetzt und eingeleitet von Otto Sittig, Prag. Paper. Pp. 145. Price, Mark 8.40. Berlin: S. Karger, 1926.

The name of Hughlings Jackson is a household word in neurologic circles throughout the world today when the full significance of his observations and the generalizations he made from them are beginning to be appreciated. Few, however, have the opportunity to refer to the original writings of the "Father of English Neurology," many of which appeared in journals of small circulation. In the volume under review is reprinted the classic "A Study of Convulsions" which was published in *Transactions of the St. Andrews Medical Graduates' Association*, 1869, pp. 162-204. The original English is given on one page and the German translation on the page facing it. In the introduction, Dr. Sittig states that the object of this work is to familiarize German neurologists with the genius and method of Hughlings Jackson, who was characterized by Arnold Pick as the "profoundest thinker in neuropathology." A brief sketch of Jackson's life and work, which pays sincere tribute to the simplicity, honesty of observation and keen thinking of the great master, prepared with the aid of Henry Head of London, provides a fitting prelude to the main article.